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SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

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SURGERY

VOL. 34 OCTOBER, 1953 No. 4

Original Communications

RESULTS OF OPERATIVE TREATMENT OF ACUTE PERFORATED PEPTIC ULCER

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IN THE past several years many reports have appeared in the literature concerning the operative and nonoperative methods of treatment for acute perforated peptic ulcer. The mortality in both groups is a subject for further evaluation. The series reported of the nonoperative treatment are comparatively small and, in many instances, limited to a select group of patients.[2, 13, 14] Therefore, from a statistical analysis, a fair comparison of these two methods of therapy cannot be made at this time.

A review of the current literature on the results of the operative method of treatment revealed a mortality from 1.1 to 30 per cent and a complication rate from 12 to 42 per cent.[1, 3, 10-12, 15, 17] The most frequent types of complications were those involving the wound, such as infection and evisceration, the reported incidence being, in some series, 25 to 42 per cent. Pulmonary complications were also high, ranging from 17 to 32 per cent. Peritonitis and abscess formation were reported in 12 to 32 per cent. There has been a steady decline in the mortality and complication rates during the past five years. This has been due to a combination of several factors such as earlier surgical intervention, better anesthesia, a smaller abdominal incision, use of antibiotics, and proper and adequate pre- and postoperative management.

This report is presented at this time to show that the complications and mortality rates can be extremely low as a result of the factors enumerated. This series includes 56 consecutive male patients who were operated upon for a perforated peptic gastric, or duodenal ulcer at this hospital between 1946 and 1952.

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RESULTS

The patients ranged in age from 22 to 72 years; the average age was 44 years. The greatest number of ulcers occurred in patients in the 31-to-40 and 51-to-60 age groups (Table I).

TABLE I. AGE INCIDENCE

AGE	NUMBER OF PATIENTS	PER CENT
20-30	8	14
31-40	20	36
41-50	6	11
51-60	15	27
61-70	6	10.2
Over 70	1	1.8
Total	56	100

The average interval between the time of perforation and the time the closure of the perforation was accomplished was 9.5 hours. The longest time interval was 120 hours. The number of patients operated upon within six hours following the acute perforation was 33 (58.9 per cent), and the number after six hours and after twelve hours was 14 (25 per cent) and 9 (15.9 per cent), respectively (Table II).

TABLE II. TIME INTERVAL BETWEEN PERFORATION AND SURGERY

TIME INTERVAL (HOURS)	NUMBER OF PATIENTS	PER CENT
0- 6	33	58.9
7-12	14	25.0
13-18	4	7.1
19-24	1	1.7
Over 24	4	7.1
Total	56	100

The average time interval according to age groups is noted in Table III. The highest average time interval was in the group of patients in the 21-to-30 age range.

TABLE III. TIME INTERVAL FROM PERFORATION TO SURGERY ACCORDING TO AGE GROUPS

AGE GROUPS	TIME INTERVAL (HOURS)		
	AVERAGE	LONGEST	SHORTEST
21-30	20.6	120	4
31-40	8	26	3
41-50	7	14	3
51-60	7	15	3
61-70	9	12	5
Over 70	6	6	6

The average duration of symptoms in this group of patients was 5.5 years. However, in 11 patients (19 per cent), the first indication of a peptic ulcer was the acute episode due to perforation. There was a history of bleeding from the ulcer in 18, or 32 per cent, of the patients. In 29 (51 per cent) patients, the perforation followed alcoholic inbibing. In 6 (10 per cent) patients, there was a history of a previous perforation; in 1, it had occurred twice before.

After admission and prior to surgery, the patients had a complete and thorough work-up. They were treated for shock, gastric intubation and suction were instituted early, x-ray pictures were taken, and other laboratory procedures were performed when indicated. All patients received penicillin; however, in the early group from 1946 to 1948, some patients received sulfadiazine. In recent years, Aureomycin or streptomycin was also administered. Penicillin and/or streptomycin were instilled into the peritoneal cavity prior to closure of the abdominal wound.

Most of the patients were given inhalation anesthesia. A short right transverse incision above the umbilicus, dividing the right anterior and posterior rectus sheaths transversely, was performed on 50 (89 per cent) patients. The right rectus muscle was transected. In the remaining 6 (11 per cent) patients, a short right vertical pararectal or paramedian supraumbilical incision was employed. These wounds were closed with catgut in 27 patients (48 per cent); with silk in 27 (48 per cent); and with fine wire in 2 (4 per cent). Drainage of the wound was not performed. All wounds healed by primary intention, except one in which a wound infection occurred. Wound dehiscence or postoperative hernia did not occur.

In this series of fifty-six cases of perforated peptic ulcer, thirty-eight (68 per cent) were located in the first portion of the duodenum, eleven (20 per cent) were benign gastric ulcers, and seven (12 per cent) were described as pyloric ulcers. Because of edema, induration, and loss of normal landmarks, the operating surgeon was often unable to state definitely whether the ulcer was gastric or duodenal; hence, the designation pyloric ulcer was made. Biopsies were taken of most of the gastric lesions, and no malignancy was found microscopically.

In fifty-three (94 per cent) of the perforations, closure was accomplished by interrupted catgut sutures of the Lembert type tied over a pedical omental graft. In one case, a purse-string suture reinforced with interrupted Lembert sutures was used and, in the remaining two cases, the round ligament and omentum were sutured over the defect. In the last two cases the defect was too large and the surrounding tissue too indurated and friable for satisfactory closure without the danger of postoperative pyloric obstruction.

The fluid and exudate in the peritoneal cavity as a result of peritonitis and spillage of gastric and duodenal contents were aspirated. In only one case was the peritoneal cavity drained, and this was accomplished through a stab wound. The fluid and material obtained from the peritoneal cavity in the majority of instances were sent to the laboratory for culture. The cultures were positive in only four cases. No correlation was noted between positive cultures and the time interval before treatment or development of postoperative complications in this series of cases.

There were *no deaths* in the entire series.

The patients treated during the 1946 to 1948 period were ambulatory on the second to the fourth postoperative day. After 1948, all patients were ambulatory on the first day.

Nasogastric suction was continued for from three to four days following surgery in the uncomplicated group of patients. Oral feedings were begun

usually by the third or fourth postoperative day. The patient then received a progressive gastric diet.

Early postoperative complications developed in 12 (21.4 per cent) patients (Table IV). A pelvic abscess occurred in one patient 61 years old, and wound infection occurred in another. Three patients developed pyloric obstruction necessitating a partial gastrectomy three weeks following the acute perforation. In 3 patients, further bleeding occurred following closure of the perforation. This subsided under further conservative treatment.

TABLE IV. EARLY POSTOPERATIVE COMPLICATIONS

TYPE OF COMPLICATION	NUMBER OF PATIENTS	PER CENT
Pelvic abscess	1	1.8
Gastrointestinal bleeding	3	5.3
Cardiac decompensation	1	1.8
Severe distention	1	1.8
Pleural effusion	1	1.8
Wound infection	1	1.8
Pyloric obstruction	3	5.3
Esophageal perforation	1	1.8
Total	12	21.4

The average hospital stay of the patients who developed no serious complications, which included most of the patients in this series, was sixteen days.

All patients were recalled twenty-eight days after the initial discharge from the hospital for further studies. The patients with no complications were treated thereafter medically.

Of the 53 patients in this category, 17 (32 per cent) required further treatment. Eleven of the 17 required partial gastrectomy. Therefore, 14 patients of the original 56 required subsequent partial gastrectomy following perforation due to complications of the disease per se, such as pyloric obstruction, gastrointestinal bleeding, or failure to respond to medical treatment. This represents the need for definitive surgery at this time for 25 per cent of the patients in the entire series.

COMMENT

In general, both the reports in the era of 1930 to 1942 and the recent reports indicate significantly high morbidity and mortality rates. However, in recent years these have been substantially reduced. It is our opinion, from the study of our cases, that these two factors can be more readily controlled and brought within the range of the results of other acute surgical conditions.

These two factors can be favorably influenced today by institution of definitive surgery at an earlier period following perforation, by thorough pre- and postoperative management, by the use of antibiotics, proper anesthesia, and a short anatomically placed abdominal incision closed with nonabsorbable suture without drainage, by early ambulation, and by early oral feedings.

SUMMARY AND CONCLUSIONS

The results of the operative treatment of acute perforated peptic ulcer in 56 consecutive male patients are presented. The patients ranged from 22 to

72 years in age. The average time interval from acute perforation to surgical closure of the defect was from 20.6 hours to 6 hours in the third decade to the eighth decade, respectively. The over-all average time interval was 9.5 hours. A small transverse right supraumbilical incision was employed in most cases. Silk closure of the wound was accomplished. The patients were ambulatory on the first to the third postoperative day. Dehiscence and postoperative herniation did not occur.

Neither the peritoneal cavity nor the wound was drained. A pelvic abscess developed in only one case. *There were no deaths.*

The patients were treated by nasogastric suction for from three to four days; penicillin, Aureomycin, or streptomycin was administered.

A careful follow-up was conducted. Twenty-five per cent of these patients required partial gastrectomy at a later date; this was necessary as a result of pyloric obstruction, gastrointestinal bleeding, or failure to respond to medical treatment.

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AUTOPSY SURVEY OF PEPTIC ULCER ASSOCIATED WITH OTHER DISEASE

A Review of Related Etiological Factors Concerned

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INTRODUCTION

THE voluminous clinical, statistical, and experimental investigations that are contributed on the subject of peptic ulcer attest to its bewildering pathogenesis; a recapitulation of this literature serves only to stress the basic fact that no single factor can be held responsible. Because gastroduodenal ulcers usually recur following healing, a constitutional predisposition, a diathesis, is postulated to obtain in afflicted individuals, although it cannot be definitely stated what underlying abnormality is responsible for such predisposition. And, undoubtedly, the ulcer diathesis alone is not sufficient to produce a mucosal ulceration of the stomach or duodenum. There must be, in addition, precipitating factors, items promoting or abetting the ulcer diathesis.

Of many precipitating factors which allegedly play a role in the genesis of ulcer, the acid-peptic digestive factor is of prime importance. The concept that there is no ulcer without free hydrochloric acid has come to be accepted. More recently, experimental observations, which will be enumerated later, have served to re-emphasize the role of vascular factors in abetting the ulcer diathesis. Although ulceration may follow disturbances of the vascular supply to the stomach or duodenum without augmenting gastric secretion, an interrelationship between the acid-peptic and vascular factors exists; ulceration does not occur without the acid-peptic digestive mixture gliding over the gastric or duodenal mucous membrane.

The following presentation embodies a study of the occurrence of peptic ulceration in certain disease entities and a review of the factors which may abet the genesis of such ulceration. It was anticipated that a preliminary statement regarding the frequence of peptic ulcer, as reported in routine series of necropsies, might serve as a base line in evaluating the incidence of ulcer complicating the disease states investigated. However, the literature on the subject revealed that no uniformity of opinion exists. According to autopsy records, the reported incidence of petpic ulcer in individuals dying from all causes has varied from 1.8 per cent[1] to 12.2 per cent[2, 3] and higher[4] in series large enough to be statistically significant; the average appears to be about 5 per cent,[5] although this seems quite high. The comparative incidence of gastric to duodenal ulceration is also difficult of analysis. Duodenal ulceration appeared to be a rare

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pathologic entity in the nineteenth century. At the turn of the century the necropsy ratio of gastric to duodenal ulcer was at high as 20:1, while records at the present time indicate that gastric and duodenal ulceration occur with about the same frequency.

To better evaluate the incidence of peptic ulceration in the disease entities studied, a control series of 1,000 consecutive autopsies, from the 1942 files of the University of Minnesota Department of Pathology, was reviewed. Of these, forty were found to present an erosion or ulcer of the gastric or duodenal mucosa. In no case was an erosion or ulcer interpreted as being the result of postmortem autolysis, unless this was specifically noted in the record by the examining pathologist; of the forty cases, however, at least five suggested, from the description of the erosion and the time interval between death and necropsy, that the mucosal change observed was autolytic in nature.

Of the forty cases in which gastroduodenal erosion or ulcer was exhibited, there were eight (.8 per cent) in which peptic ulceration caused death primarily by perforation or hemorrhage; these should be excluded from a control series. In the remaining thirty-two cases, gastric or duodenal erosion or ulcer was presented as a finding which was associated with other primary pathologic lesions causing death, an incidence of 3.2 per cent. Significantly, in these thirty-two cases, there was a primary diagnosis of coronary occlusion, hypertensive heart disease, or generalized arteriosclerosis in eleven (37.5 per cent); there was a primary diagnosis of fracture of the femur in one. The mucosal pathology was localized in the duodenum in sixteen and in the stomach in thirteen, and concurrent gastric and duodenal ulceration was present in three.

REVIEW OF THE LITERATURE AND ORIGINAL OBSERVATIONS

Burns.—The occurrence of ulcer in the stomach and duodenum following burns has been recognized for more than 100 years. Curling[6] in 1842 first described duodenal ulceration associated with burns as a clinical entity, although even before that Swan (1823), Dupuytren (1833), Cooper (1839), and Long (1840) had reported ulceration of the stomach and duodenum following burns. The ulceration, as Curling described it in the ten cases reported, is of an acute character, the immediate causes of death being perforation with subsequent peritonitis and penetration with hemorrhage.

There is no uniformity of opinion regarding the incidence of Curling's ulcer although its occurrence is generally accepted as being more common than coincidence would allow. Harkins,[7] in an exhaustive review of the literature, found thirteen authors with wide necropsy experience who reported that they had never seen duodenal ulcer following burns. However, statistical analysis, as pointed out by Harkins, is subject to error in determining the frequency of the lesion; many patients dying within the first few hours after a burn, or even later, are not suspected of having peptic ulceration and no autopsy is performed, and there are no statistics available as to the percentage of ulcers following burns in patients who go on to recovery. In Harkins's collected series of 680 burn necropsies reported in the literature from 1840 to 1937, there were twenty-six cases in which gastric or duodenal ulceration was presented. The percentage frequency of ulceration in individual series varied from 0 per cent to 36 per cent; the average incidence of 3.8 per cent agrees fairly well with the conclusion of Perry and Shaw[8] and is probably as accurate an estimation as can be determined. The gastrointestinal ulceration occurring in burns is usually located in the duodenum and in most instances where gastric ulcers are found they are associated with duodenal ulceration. The ratio of duodenal ulcer to gastric ulcer in various collected series was 4.5:1.

The mechanism of the production of Curling's ulcer is not yet fully understood, although most of the pathogenic factors involved are being subjected to investigation and interpretation in the light of present knowledge of the pathologic physiology of burns and ulcer. A review of the literature reveals that theories of causation are almost as numerous as the investigators reporting interpretations. The older concepts, such as Curling's theory of overactivity of Brunner's glands, Brown-Séquard's spinal reflex hypothesis, etc., are now largely discounted by modern investigators.

Billroth in 1867 and Moynihan in 1912,[9] as well as many others, attributed the ulcers to an embolic process from septic foci; they noted that similar ulceration had been reported in cases of sepsis not caused by a burn and that ulcers usually occurred when the burned area was undergoing septic changes. Perry and Shaw,[8] in a study of duodenal disease reported from Guy's Hospital, recorded a ratio of eighteen septic ulcers to fifty-two from all causes, and concluded that duodenal ulceration is associated with septic conditions nearly as frequently as it is with burns. However, Friesen,[10] working with dogs, found that the administration of penicillin did not decrease the incidence of ulcers in dogs subjected to third degree burns of 40 per cent of the surface area. He also demonstrated that thrombi and fibrin emboli are not factors in the genesis of these ulcers; the incidence of ulcer in burned animals given dicumarol was identical with that in control animals.

The assumption that a toxin, elaborated in the burned skin and circulated by the blood, is the causative agent in the production of the ulceration has been prevalent for many years. The literature is voluminous, and opinions as to the specific nature of the toxic substance are as diverse as the number of reports. However, there is some evidence that histamine or a related compound is liberated in the skin of human beings, dogs, and other animals under the influence of thermal trauma. Levin[11] in 1929 postulated histamine or a histaminelike substance to be the special toxin of burns, and he believed that the combination of hyperacidity and the devitalizing effect of the toxin on the mucous membrane favored the development of the ulcer. Necheles and Olson[12-14] found a great increase in gastric motility in a number of burned animals as well as a considerable increase in the volume and acidity of gastric secretion. They believed that a histaminelike substance liberated by the burn was responsible for the increase in gastric acidity and that the increase in motility might be due to the liberation of a compound similar to acetylcholine. On the contrary, Hartman in 1945[15] found that the free and total acidity in his experimental animals reduced sharply after the burn, and Wilson,[16] in gastric analysis in burn patients, failed to demonstrate any excessive gastric acidity. Rose and Browne,[17] studying the blood histamine in severely burned patients, found an increase in blood histamine within one hour after the burn, but in all cases the histamine level decreased with the appearance of toxemia and edema. Kapsinow,[18] in a study of toxins elaborated by burned tissue, found that extracts of normal skin were also toxic; analysis of the supposed toxic fraction revealed that what had been considered the burn toxin was merely alcohol, incompletely extracted, and he believed that this error, handed down through the literature, accounted for the toxin theory. Kapsinow also showed that other substances were poorly absorbed when injected into burned areas, and he believed that any toxin formed in such areas would be absorbed as sparingly.

The decreased blood volume in burned animals was demonstrated by Blalock.[19] The occurrence of hemoconcentration following burns in man is well known; hemoconcentration provokes failing circulation, inefficiency of the blood as an oxygen carrier, oxygen starvation of tissues, and finally suspension of circulation and death of the tissues. Kapsinow in 1934[18] was one of the first to stress these factors in the genesis of Curling's ulcer. He found that, in burned animals, the frequency of ulcer was decidedly less if the blood concentration was kept controlled, and he postulated that stasis of the blood with rupture of the capillaries underlying the duodenal mucosa produced tissue anoxia, necrosis, and ulceration. Hartman[15] found that burned animals treated by tanning, thereby losing less plasma, developed gastric or duodenal ulcers much less frequently than those not tanned. Cope and Rhinelander,[20] in studying victims of the Cocoanut Grove fire, believed

it possible that the ulcerations occurring in their patients resulted from anoxia of mucosal surfaces due to capillary stasis; they considered the incidence of intestinal ulceration and hemorrhage inversely proportional to the success of the shock therapy. Friesen,[10] however, has shown in controlled experiments that shock need not be present for the accelerated production of histamine-provoked ulceration in burned animals; in dogs suffering a 40 per cent burn, ulceration developed even though serial blood pressure readings were maintained within normal limits. He found that by preventing hemoconcentration by the administration of plasma, gastrointestinal ulceration in burned animals did not occur. The incidence of gastrointestinal congestion, erosion or ulcer in his burned animals was directly proportional to the incidence and degree of hemoconcentration.

That stasis of the blood in the gastroduodenal vascular bed can result in gastroduodenal erosions and ulcers in pathologic conditions other than burns has been demonstrated. Baronofsky and Wangensteen[21] created partial obstructions to the normal venous return of blood from the stomach in rabbits and dogs, and they found that erosions and ulcers were far more readily provoked with histamine; the mucosal congestion brought about by venous stasis predisposed the gastric mucosa to erosion by the acid-peptic digestive activity of the gastric juice. The same authors similarly demonstrated that nitroglycerin accelerated the occurrence of the histamine-provoked ulcer in rabbits and dogs[22]; the effect of the nitroglycerin in dilating the smaller splanchnic vessels, a venous-pooling effect, was considered the primary mechanism involved.

A review of the autopsy records of the Department of Pathology, University of Minnesota, revealed that, from 1926 to 1944, 156 necropsies had been performed on persons dying of burns. Of these, six (3.8 per cent) exhibited acute gastrointestinal findings consisting of duodenal ulcerations (two), multiple gastric ulcerations (one), hemorrhagic gastric mucosa associated with gastric bleeding (two), and hemorrhagic mucosal change, associated with gastrointestinal bleeding, in the stomach and small bowel (one). Other cases (five) of gastric mucosal change were present in the series but were excluded as being due to post-mortem autolysis. From a review of the case records, it was not possible to draw any conclusions regarding the factors involved in the pathogenesis of the mucosal change exhibited. All patients presenting gastrointestinal pathology were children; it is probable that this is due to the higher incidence of burns in children. However, that all those presenting such mucosal change were children is remarkable in that peptic ulcer is a rarity in this age group. Infection of the burned areas was present in three of the six cases. Unfortunately, recorded data were not sufficient to evaluate the etiological importance of hemoconcentration and its associated gastrointestinal vascular stasis. Case summaries are listed in Table I.

Arterial Disease.—Virchow in 1853[23] was the first to emphasize the apparent relation of local vascular disturbances to gastric ulcer. It was his belief that the ulceration was preceded by a hemorrhagic necrosis of the mucous membrane; this he attributed to vascular lesions, mentioning disease, obstruction, and spasm of the arteries. Merkel in 1865[24] was one of the first to cite cases of gastric ulcer in which vascular lesions were actually demonstrated; this work was confirmed by Hauser in 1883.[25] Hauser was also the first to call atention to the fact that gastric ulcers were frequently associated with general arteriosclerosis; in reviewing necropsy material, he found that gastric ulcer, in the majority of cases, occurred after the age of 30 years. During the remainder of the nineteenth century, there were many other published reports confirming Hauser's original demonstration of gastric arteriosclerosis. Lewin in 1908[26] cited similar cases and, in a review of the literature, concluded that arteriosclerosis of the stomach may occur in young people and that severe arteriosclerosis of the stomach may occur with only slight atheromatous changes in the aorta and other vessels. Ophüls in 1913[27] found the common occurrence of gastric or duodenal ulcer in patients with arteriosclerosis so evident that he began to look on it as a lesion comparable to arteriosclerotic scars in the heart or kidney. More recently, Wangensteen,[28] in discussing the vascular factor in ulcer genesis, cited additional cases of hematemesis and melena from erosive and ulcerative gastric lesions associated with arteriosclerotic changes in the gastric arteries.

TABLE I. SUMMARY OF CASES PRESENTING ACUTE GASTROINTESTINAL ULCER AND/OR EROSION IN PATIENTS DYING OF BURNS

PATIENT	AGE (YR.)	SEX	EXTENT OF BURN (PER CENT)	CLINICAL EVIDENCE OF GASTROINTESTINAL HEMORRHAGE (+ OR −)	TIME INTERVAL BETWEEN BURN AND DEATH (DAYS)	GASTROINTESTINAL FINDINGS AT AUTOPSY	REMARKS
R. H.	13	F	60	−	12	Multiple superficial gastric ulcers localized in fundus	Infection under eschar
D. W.	13	M	60	+	25	Posterior and anterior duodenal ulcers, 1 to 1.5 cm.	Infection under eschar; septicemia
L. R.	2	F	40	−	12	Posterolateral duodenal ulcer, 2 cm., with perforation	Infection under eschar
D. S.	8	F	50	+	2	Hemorrhagic mucosa in proximal one-half of stomach with blood in stomach and small bowel	—
O. T.	4	M	35	−	4	Entire gastric mucosa hemorrhagic; hemorrhagic area in jejunum. Stomach filled with old blood	—
B. A.	2	F	50	+	5	Hemorrhagic areas throughout mucosa of stomach and most of small bowel; fresh blood in stomach and small bowel	—

From a histopathologic viewpoint, however, the role of arterial disease as an abetting factor in the genesis of ulcer is a confused issue. There are those who, although admitting the frequence of arterial obstructive changes at the base of the ulcer and the incidence of arteriosclerosis in the arteries which supply the ulcer cite, believe that these changes are the result of the ulcerative process. Schultz in 1931,[29] in a study of thirty ulcers, found coexisting arterial obstructive lesions in every case, but he presented evidence that the arterial lesions corresponded in age with the age of the ulcer. Hebbel[30] shared the view that the arterial lesions associated with ulcer are a secondary phenomenon; in a study of several hundred stomachs, he observed arteriosclerotic change in the intrinsic gastric vessels on but rare occasions other than those associated with an ulcer floor. Other investigators such as Wilkie in 1911,[31] Ophüls in 1913,[27] and others emphasized the frequency of arteriosclerosis in the arteries which supply the ulcer site, and Fetterman in 1935[32] stressed the marked intimal thickening of the vessels in areas both remote and adjacent to the gastric ulcers in each of his patients.

A knowledge of the blood supply of the gastric and duodenal mucous membrane is fundamental in evaluating the vascular factor in the genesis of ulcer. Anatomically it has been pointed out by Ophüls[27] and again by Einhorn[33] that those parts of the wall of the stomach and duodenum where ulcers usually occur are poorly supplied with arteries. This is particularly true of the pyloric end of the stomach, at the lesser curvature and on the posterior wall, and of the beginning of the duodenum at its convexity. Wilkie,[31] in a study of the blood supply of the first part of the duodenum, also found the arterial supply far from abundant, and Disse[34] and Reeves[35] have demonstrated that the submucosal arteries of the stomach and duodenum become end arteries as they enter the mucosa; each of these terminal vessels supplies an area of mucosa measuring approxi-

mately 2.5 mm. in diameter. Reeves also found that the submucosal arteries along the lesser curvature of the stomach and first one inch of the duodenum are more tortuous, narrower, and less numerous than elsewhere.

The production of peptic ulceration by experimental arterial spasm and obstruction suggests the importance of the vascular factor in ulcer genesis. Panum as far back as 1862[36] produced an acute gastric ulcer in a dog by injecting black wax into the crural artery, the wax being demonstrable in the terminal vessels leading to the resultant black fundic ulcer. The investigations of Payr in 1910[37] revealed that gastric ulcers followed the experimental production of gastric endarteritis obliterans, and Honda in 1927[38] produced ulcers by injecting sterile emboli into various gastric arteries. Rosenbach[39] was probably the first to demonstrate, in 1883, that gastric ulceration followed prolonged vasoconstriction. More recently, vasospastic agents such as epinephrine and Pitressin have been used to produce gastric and duodenal ulceration in experimental animals. Baronofsky and Wangensteen in 1945[40] confirmed the results of previous investigators using these agents to produce peptic ulceration; they also demonstrated, in Heidenhain and Pavlov pouch dogs, that Pitressin and epinephrine did not augment gastric secretion.

The importance of the vascular factor in the ulcer diathesis has, by virtue of these and other studies (portal hypertension, nitroglycerin, fat emboli), recently been re-emphasized. The frequency with which a bleeding ulcer first becomes manifest in individuals in the sixth or seventh decade is common clinical knowledge. Wangensteen in the 1945 Listerian Oration[28] cited the problem of why, if the acid-peptic factor is the determinant in ulcer genesis and if such patients harbor an ulcer diathesis, they did not manifest symptoms earlier in life. A logical explanation based on the previously documented facts concerning gastric and duodenal atherosclerosis, vascular anatomy, and experimental production of peptic ulceration would include a consideration of vascular disease of the vessels supplying the stomach and duodenum, particularly the terminal vessels. The narrowing or plugging of such vessels, resulting in localized areas of mucosal ischemia, invites erosion of the involved mucosa by the acid-peptic digestive action of the gastric juice.

To evaluate one small aspect of the vascular factor in ulcer genesis, the incidence of peptic ulcer in patients dying of coronary occlusion and hypertensive heart disease was studied. Although the incidence of arteriosclerosis of the gastric and duodenal vessels might be inferred to be higher in these two disease groups than in other disease entities, there is no objective evidence to support the inference. Too, it is recognized that the mechanism of production of peptic ulceration associated with these disease states might involve many factors other than atherosclerotic occlusion or narrowing of the end vessels supplying the gastric and duodenal mucosa. Of the vascular factors alone, a reflex spasm of the gastric vessels secondary to coronary closure or venous stasis in the gastroduodenal vessels associated with the back pressure from a failing heart might conceivably play a role. In the cases to be presented, no observations were made relative to the presence or absence of atherosclerotic change in the intrinsic gastroduodenal arteries.

In a review of the literature, I have been able to find only one reference reviewing the incidence of peptic ulcer in coronary disease. Walsh and co-workers,[41] in 1941 in a clinical study of 1,000 patients with coronary disease, found clear evidence of peptic ulcer in twenty-seven (2.7 per cent) cases. They also found, in a study of 2,737 necropsies of persons 20 years or older dying of all causes, 149 (5 per cent) patients with peptic ulcer; of these 149, 30 (20 per cent) had well-marked coronary disease. However, the same incidence of coronary disease was noted in the remaining 2,588 patients without peptic ulcer. They also found that peptic ulcer occurred in 30 (5 per cent) of the 576 patients with coronary disease and with equal frequency (5.5 per cent) among the 1,222 patients without coronary disease. They concluded that there was no significant association of peptic ulcer and coronary disease in the same person. In a discussion of their paper, however, Boas disagreed; from his clinical experience, he believed that it was conceivable for the same arterial disease or insult to manifest itself simultaneously in a coronary and gastric artery.

TABLE II. SUMMARY OF CASES PRESENTING GASTRODUODENAL ULCERATION IN PATIENTS DYING OF CORONARY OCCLUSION

PATIENT	AGE (YR.)	SEX	CARDIAC LESION	CLINICAL EVIDENCE OF GASTROINTESTINAL HEMORRHAGE (+ OR −)	TIME INTERVAL BETWEEN OCCLUSION AND DEATH (DAYS)	GASTROINTESTINAL FINDINGS AT AUTOPSY	REMARKS
T. H.	53	F	Thrombosis, anterior descending branch of left coronary artery	−	2	Posterior duodenal ulcer, 1 cm.	Pernicious anemia. Cardiac decompensation
C. L.	52	M	Thrombosis, anterior descending branch of left coronary artery	−	42	Posterior duodenal ulcer	Cardiac decompensation
J. O.	51	M	Thrombosis, anterior descending branch of left coronary artery. Mitral stenosis	−	21	Three superficial ulcers on greater curvature of fundus. Healed prepyloric ulcer	Cardiac decompensation. Infarcts, lung and spleen
V. M.	66	M	Thrombosis, anterior descending branch of left coronary artery	−	12	Gastric ulcer, lesser curvature, 1 cm., surrounded by multiple acute ulcers	Cardiac decompensation. Infarcts, spleen and kidney
F. V.	67	M	Thrombosis, right coronary artery	−	14	Multiple small irregular duodenal ulcers	Cardiac decompensation. Infarcts, spleen and kidney
W. D.	60	M	Thrombosis, anterior descending branch of left coronary artery	−	2	Posterior duodenal ulcer, 1 cm.	Cardiac decompensation. Infarcts, spleen and kidney
J. B.	60	M	Thrombosis, left coronary artery	−	4	Anterior duodenal ulcer, 8 mm., close to perforation	Cardiac decompensation. Infarcts, spleen and kidney
P. K.	81	M	Thrombosis, anterior descending branch of left coronary and right coronary arteries	−	?	Two prepyloric ulcers, 1.5 and 2 cm.	Cardiac decompensation. Infarcts, spleen and kidney
T. C.	53	M	Thrombosis, right coronary artery	+	3	Duodenal ulcer, 1 cm.	Cardiac decompensation. Infarcts, spleen and kidney
C. M.	42	M	Thrombosis, anterior descending branch of left coronary	−	9	Perforating prepyloric ulcer, 4 by 3 cm.	Cardiac decompensation. Multiple infarcts, lungs and spleen
E. B.	63	M	Thrombosis, anterior descending branch of left coronary	+	3	Prepyloric ulcers, 3 cm., 1 cm., and 6 mm.	Passive congestion, all viscera
J. H.	69	M	Thrombosis, left coronary	−	50	Three prepyloric ulcers, 1 to 5 mm.	Passive congestion, all viscera
F. M.	77	M	Thrombosis, anterior descending branch of left coronary	+	2	Prepyloric ulcer, 4.2 cm.	Passive congestion, all viscera

It is interesting to note in passing that Ivy,[5] charting the monthly mortality rates of peptic ulcer, coronary disease, and cerebral vascular disease over a five-year period, found that, with the exception of February, the mortality curves of these entities conformed.

Using the records of the Department of Pathology, University of Minnesota, a study was made of the incidence of peptic ulcer in patients dying of coronary occlusion. In 1943, from a total of 2,467 necropsies performed, 168 consecutive cases, in which death was due to coronary occlusion, were reviewed. Of these, thirteen patients presented peptic ulceration, an incidence of 7.7 per cent. Only three of these patients, as indicated by the records, gave a previous history of symptoms referable to the upper gastrointestinal tract. From the description, the majority (nine) of the ulcers were acute. Six were localized in the stomach and seven occurred in the duodenum. Case summaries are listed in Table II.

A similar study was made of the incidence of peptic ulcer in patients dying of hypertensive heart disease. In 1936, from a total of 2,446 autopsies performed, 116 consecutive cases with a primary diagnosis of hypertensive heart disease were reviewed. Of these, in five (4.3 per cent) peptic ulceration was presented; in two, multiple ulcers were present in both stomach and duodenum, while in the remaining the process was localized in the stomach in two, in the duodenum in one. It was of added interest to note the frequency with which mucosal change in the stomach, aside from ulceration, was described; in fourteen cases (12.1 per cent), excluding those in which autolysis might have been a factor, the gastric mucosa was variously described as "hemorrhagic," "intensely inflamed," or "markedly congested." This change, I believe, is significant, although any attempt at explanation would be mere conjecture. Case summaries are listed in Table III.

TABLE III. SUMMARY OF CASES PRESENTING GASTRODUODENAL ULCERATION IN PATIENTS DYING OF HYPERTENSIVE HEART DISEASE

PATIENT	AGE (YR.)	SEX	DURATION AND MAGNITUDE OF HYPERTENSION	DURATION OF DECOMPENSATION (DAYS)	CLINICAL EVIDENCE OF GASTROINTESTINAL HEMORRHAGE (+ OR −)	GASTROINTESTINAL FINDINGS AT AUTOPSY	REMARKS
J. T.	56	M	10 yr., BP = 220/92	14	−	Pyloric ulcer, 5 by 3 mm., duodenal ulcer, 2 cm.	Chronic passive congestion, all organs
S. G.	85	M	15 yr., BP = 210/120	60	−	Two small acute duodenal ulcers	Chronic passive congestion, ascites
W. M.	77	M	6 yr., BP = 200/100	70	+	Three prepyloric ulcers, .5 to 1 cm., healed duodenal ulcer	Chronic passive congestion, all organs
M. N.	65	F	5 yr., BP = 230/120	40	−	Small gastric ulcer, lesser curvature	Chronic passive congestion, all organs
E. C.	50	M	8 yr., BP = 220/120	10	+	Ulcer in cardia, 1 by 5 cm.	Chronic passive congestion, cerebral hemorrhage

Fracture.—All varieties of injuries to bone, particularly fractures, affecting the fatty marrow may produce fat embolism. There is no doubt that depot fat of the marrow will enter the blood stream following mechanical disturbance. The difficulty of recognizing fat embolism, both clinically and at post-mortem, results in the overlooking of many cases, and accounts for some of the wide discrepancy in the reported incidence of fat embolism secondary to fracture. It is undoubtedly true, however, that some fat is set free from the ruptured fat cells in every case of amputation or fracture of the long bones. Warthin[42]

in his classic study of fat embolism summarized his opinion in this fashion, and many subsequent thorough studies of the problem by competent investigators confirm his findings.

Fat embolism is a condition in which there is fat circulating in the blood stream in globules large enough to occlude the capillaries and induce multiple anoxemic foci. The normal blood contains no free neutral fat in droplets large enough to take the fat stains; following injury to bone marrow, free neutral fat can be demonstrated in the blood stream by various staining methods. If such fat is present, a sufficient agglomeration of particles may occur anywhere and at any time to plug a capillary; when the amount of fat liberated is small, the results may be unimportant and unnoticed, the changes produced being dependent upon the anatomic importance of the capillaries blocked. It is agreed by most investigators that there is not a single organ or tissue in the body that does not get some fat into its capillaries during a fatty embolism.

The essentials for the entry of embolic fat into the circulation are mobilized fat, disrupted and patent veins, and local pressure. Injuries to bone provide exactly the factors necessary. Scriba[43] has shown that the fat, reaching the heart and lungs first via the venous system, may filter through the lungs without difficulty; after gaining the systemic circulation, the fat may be introduced to any organ, producing changes secondary to the mechanical blockage of the lumena of capillaries and arterioles. Speculation regarding the induction of arterial spasm by the presence of fat has no basis in experimental data.[44] However, there is some experimental evidence to support the theory that the fat has a local action on the capillary wall. It has been suggested by Harris[45] that alteration in the fat, in the nature of hydrolysis by tissue lipase to fatty acids and soaps, renders it more toxic and irritating, producing a far more intense inflammatory exudate than occurs with simple blockage of the capillary lumen.

Clinically, symptoms referable to the cardiorespiratory and central nervous systems are the most common in fat embolism. Prior to 1945, little can be found in the literature relating to the occurrence of peptic ulcer in fat embolism. Wangensteen,[28] in reviewing the subject, was able to find only one allusion to it; Schridde and Schmorl, in a discussion of a paper by Sternberg,[46] each described post-mortem findings of gastric ulceration and punctate gastric mucosal hemorrhages accompanying fracture, in association with fat emboli in the submucosal gastric vessels. Warthin,[42] on the other hand, stated that fat emboli occurring in the capillaries of the stomach and intestines have not, in his experience, caused any recognizable tissue change. In five of the cases which he presented, he described fat emboli in "all the organs," specifically mentioning those in the gastric mucosa in one; there was no associated gastric or duodenal pathology, although the gastric mucosa was described as autolyzed in two. Scriba,[43] Graham,[47] and Lecount and Gauss[48] are others who described fatty emboli, associated with fracture, occurring in the vessels of the gastric mucosa; in none of their cases, however, was there associated pathology of the mucosa.

More recently Wangensteen[28] has reported four cases of fracture in which hematemesis and melena occurred as a complication. Post-mortem examination revealed an acute duodenal ulcer in one, a gastric erosion associated with multiple submucosal areas of hemorrhage in another; in the third case, a large ulcer in an 18-year-old gastroenterostomy stoma was demonstrated by roentgenogram and, in the fourth, a clinical diagnosis of acute peptic ulcer was made. In the two cases in which the patients recovered, gastrointestinal symptoms did not recur following therapy. Occasionally, in the literature, additional examples are incidentally reported. Vale and Cameron,[49] writing on gastric and duodenal perforation, described such a case in which the patient, being treated for a compound fracture of the leg, developed perforation of an acute pyloric ulcer without antecedent history of gastric symptoms. Undoubtedly, many other unrecorded illustrative examples exist.

Experimentally, it has been demonstrated that gastric and duodenal erosion and ulcer can be produced by fracture and that such lesions are associated with fat emboli in the smaller gastroduodenal vessels.[50] Merendino and associates[51] in 1945, working with

guinea pigs, cats, and dogs, demonstrated the occurrence of such upper gastrointestinal pathology in 53 per cent of animals subjected to various traumatic procedures (drilling, fracture, curettement) to bone marrow. That stimulation of gastric secretion did not occur following fracture was shown by the same authors[52] in controlled studies on human beings and dogs; it was reasoned, therefore, that a histamine effect from the fracture site did not play an etiological role in the genesis of associated erosion and ulceration of the gastric and duodenal mucosa. In 1945, Baronofsky and Wangensteen[53] demonstrated that the accelerated production of histamine-provoked gastroduodenal erosion or ulcer could be effected in rabbits, cats, and dogs by the intravenous injection of ether-extracted human fat; microscopic sections of the gastroduodenal specimens revealed fat emboli in the tissue adjacent to the ulceration. It was also determined that the rate of disappearance of fat emboli from various tissues was quite rapid; a markedly lowered incidence of demonstrable emboli in tissue section occurred after the fourth day in contrast to the incidence during the preceding days; in the stomach, the incidence of demonstrable emboli decreased from 47.8 to 3.7 per cent after the fourth day.

Work on the experimental production of ulcer by agents causing chronic arterial spasm, discussed in the section on arterial disease, has indicated that the production of even temporary areas of anemia in the gastric or duodenal mucosa renders these areas prone to injury by the gastric juice. In the same manner, fat emboli, released into the blood stream following fracture, may occlude the end vessels in the gastric and duodenal mucosa, causing areas of local anemia which are less resistant to the acid-peptic juice. This, then, defines a mechanism by which gastroduodenal erosion or ulceration may occur when associated with fracture. The rapidity of the disappearance of the fat from the mucosal and submucosal vessels probably accounts for the fact that erosion or ulceration has not been more commonly observed accompanying fracture of the long bones in man.

In an attempt to correlate the incidence of acute peptic ulcer associated with fractures of the long bones, a review was made of the records of such fractures in the files of the Pathology Department of the University of Minnesota. Skull fractures, comprising the commonest type of fracture in most autopsy series, were not reviewed; although trauma to cancellous bone can produce fat emboli,[42, 44] this is not common. Too, the etiological factors involved in the occurrence of peptic ulcer in head trauma may be complex, particularly, as Cushing[54] has suggested, if the interbrain is involved.

From 1932 to 1944 there were 375 autopsies performed on persons who expired with fractures of the long bones. Of these, eight presented concomitant acute peptic ulcer, an incidence of 2.16 per cent. In addition, there were two cases in which gastric erosion and mucosal hemorrhage were present; autolysis as the cause of this change could not be ruled out and, as a consequence, these cases were excluded. In two other cases in the series chronic peptic ulcers associated with an antecedent history of ulcer were presented; as there was no evidence of activity of the lesions at the time of death, they were not included.

Of the acute ulcers, six were localized in the duodenum. In the other two cases multiple gastric ulceration was presented. In six of the eight cases, the site of fracture was the femur. There was nothing in any of the case histories to indicate that fat embolism had been searched for or recognized clinically. Similarly, no mention of fat embolism in any organ was made by the examining pathologists, although no attempt to establish such a diagnosis was made.

Case summaries are presented in Table IV.

Chronic Ulcerative Colitis.—Chronic nonspecific ulcerative colitis, as a disease entity, was first described by Wilks[55] in 1875. It has been variously defined but, in short, its etiology is undetermined and it cannot even be definitely stated that it is a distinct entity.

The confusion attending the etiology and pathogenesis of the syndrome is marked. Ginsberg and Ivy,[56] in a critical review of experimental and clinical observations concerning the condition, discussed nine possible etiologic factors involved; listed, these are bacteriologic, allergic, traumatic, vascular, lymphatic, toxemic, metabolic, endocrinopathic,

TABLE IV. SUMMARY OF CASES PRESENTING GASTRODUODENAL ULCERATION IN PATIENTS DYING OF FRACTURES OF LONG BONES

PATIENT	AGE (YR.)	SEX	FRACTURE SITE	CLINICAL EVIDENCE OF GASTROINTESTINAL HEMORRHAGE (+ OR −)	TIME INTERVAL BETWEEN FRACTURE AND DEATH (DAYS)	GASTROINTESTINAL FINDINGS AT AUTOPSY	REMARKS
C. J.	70	F	Femoral neck	−	34	Duodenal ulcer, 5 mm.	Internal fixation with nail
P. P.	91	F	Femur, intertrochanteric	+	26	Two duodenal ulcers, 2.5 cm. and 1 cm.	Traction. Cardiac failure and pulmonary embolus
K. S.	82	F	Femur, subtrochanteric	+	14	Perforating duodenal ulcer, 1.5 by 2.5 cm.	Traction. Pneumonia
E. L.	91	M	Femoral neck	−	16	Duodenal ulcer, 1 cm.	Internal fixation. Pneumonia
R. L.	79	M	Humerus	−	19	Posterior duodenal ulcer, 1.5 cm.	Died of coronary occlusion
R. B.	63	M	Femoral neck	−	11	Several small prepyloric ulcers, 4 to 6 mm.	Traction. Paralytic ileus
J. M.	67	M	Tibia, fibula, multiple pelvic fractures	+	5	Three gastric ulcers on lesser curvature, 5 to 7 mm.	Traction. Died of exsanguination
E. H.	53	F	Tibia	−	14	Posterior duodenal ulcer, 4 mm.	Died of pulmonary embolus

and neurogenic. The pathogenesis of the condition is equally confusing. With a similar perplexity attending the problem of peptic ulceration, any attempt to relate the two etiologically would be predicated on a lack of complete understanding of either condition. However, two factors, possibly etiologically related to both diseases, deserve brief mention.

In the section dealing with vascular disease, the role of vascular spasm and occlusion in the genesis of gastroduodenal ulceration has been discussed. There is some evidence to indicate that arterial spasm may produce similar ulceration in the colon. Penner and Bernheim in 1939,[57] by the intraperitoneal injection of Adrenalin in experimental animals, produced gross changes in the ileum, colon, and gastric mucosa consisting of large ulcerations and pseudodiphtheritic membrane formation. They postulated that vasospasm, if of sufficient severity and duration, is a causative factor in the production of colonic ulceration. In addition, Ecker and Biskind[58] have shown that vasospasm undoubtedly plays a secondary role in the etiology of ulcerative colitis. In a review of the literature, however, nothing could be found pertaining to other occlusive vascular phenomenon, such as embolism or thrombosis, as agents in the genesis of large bowel ulceration.

Many writers have alluded to the emotional background in a large number of the cases of chronic ulcerative colitis and, undoubtedly, emotional disturbances such as anxiety, resentment, and guilt are, in some cases, related to the onset and exacerbations of the disease. These same types of emotional disturbances are reported to be characteristic of patients with peptic ulcer. Hypersecretion and hypermobility of the stomach may be caused in some persons by such dysphoric states and, according to Ivy,[5] the evidence presumptively supports the view that hyperactivity of the stomach may cause gastric or duodenal ulceration, although a definite conclusion is unwarranted. Such emotional disturbances also affect the motor activity of the colon in many individuals[56] causing a general increase in motility, localized or general. Lium[59] has shown, as might be anticipated from similar experiments on the stomach, that marked contraction of the colonic

musculature may cause erosions or acute ulcers of the mucosa; Willard[60] believes that the gastrointestinal hypermobility, produced by neurogenic factors, causes colonic ulceration by the action of the unresorbed, highly digestive small bowel contents on the colonic mucosa, predisposing it to secondary infection.

However, if such neurogenic factors are etiologically concerned in the production of gastric, duodenal, and colonic ulceration, they cannot be the sole factors since they are also thought to be concerned in the genesis of still other chronic disease. Ivy,[5] in analyzing the psychosomatic aspect of the etiology of peptic ulcer, stressed the fact that emotional disturbances, described as significant in the production of peptic ulcer, are also held etiologically responsible for such conditions as spastic colon, mucous colitis, and biliary dyskinesia. And, as Ginsberg[56] pointed out, it would appear that, if these emotional factors are concerned in the causation of this variety of pathologic processes, it would be necessary to postulate that the nervous centers are differentially affected or that there is a difference in the susceptibility of the stomach and colon to parasympathetic effects in various individuals.

In a review of the literature, there is little that can be found relative to the occurrence of peptic ulcer in chronic ulcerative colitis. Even such extensive reviews as that of Ricketts and Palmer[61] on the complications and associated disease accompanying chronic ulcerative colitis fail to mention peptic ulcer. The only direct reference I have been able to find is that of Bargen and Rivers.[62] In a review of 500 consecutive cases of chronic ulcerative colitis, they found sixteen (3.2 per cent) patients in whom there was convincing evidence of the concomitant presence of peptic ulcer. From their analyses of these cases, they derived presumptive evidence for an allied etiology of the two conditions. They noted an occasional periodic or even seasonal incidence of these diseases and found a parallelism between the exacerbations and remissions of each; recurrent symptoms of one condition were often associated with recurrence of the other. Also, there was evidence to suggest that therapy, if successful in relieving the symptoms of the colitis, also resulted in quiescence of the ulcer syndrome. Of the thirteen ulcers in the group demonstrated by roentgenogram, twelve were duodenal, one gastric.

The records of the Department of Pathology, University of Minnesota, show that, from 1927 through 1943, ninety-one necropsies were performed on patients dying of chronic ulcerative colitis. These cases were reviewed, and in four concomitant peptic ulceration was found to be present, an incidence of 4.3 per cent. Of these, the ulceration was limited to the stomach in two cases and was present in both stomach and duodenum in the other two.

Case summaries are presented in Table V.

TABLE V. SUMMARY OF CASES PRESENTING GASTRODUODENAL ULCERATION IN PATIENTS DYING OF CHRONIC ULCERATIVE COLITIS

PATIENT	AGE (YR.)	SEX	DURATION OF ULCERATIVE COLITIS	SYMPTOMS OF PEPTIC ULCER	GASTRODUODENAL FINDINGS AT AUTOPSY	REMARKS
S. E.	24	F	6 mo.	None	Gastric ulcer, lesser curvature, 2 by 1 cm.	Died of pneumonia one month after iliostomy
W. K.	45	M	10 yr.	None	Multiple small gastric ulcers	Died five days after iliostomy
A. J.	45	M	2 yr.	None	Multiple perforating gastric ulcers; two duodenal ulcers	Died of pneumonia
E. V.	52	M	6 mo.	None	Prepyloric ulcer and duodenal ulcer	—

SUMMARY

1. A review of 1,000 consecutive autopsies was made as a control in evaluating the incidence of peptic ulceration accompanying other disease at necropsy.

Excluding cases in which peptic ulceration caused death primarily by perforation or hemorrhage, there were thirty-two cases in which gastric or duodenal erosion or ulcer was presented as a finding associated with other primary pathologic lesions causing death, an incidence of 3.2 per cent. Of these thirty-two cases, in eleven a primary diagnosis of coronary occlusion, hypertensive heart disease, or generalized arteriosclerosis was made.

2. A review of the literature on the incidence and pathogenesis of gastrointestinal ulceration associated with burns is presented. Emphasis is placed on the relationship of hemoconcentration and stasis of the blood in the gastroduodenal vessels to the genesis of gastroduodenal ulceration in experimental animals subjected to burns. Summaries of six burn fatalities presenting acute gastrointestinal pathology are presented; these were collected from 156 burn necropsies, an incidence of 3.8 per cent.

3. The vascular factor in ulcer genesis is reviewed, emphasizing the role of atherosclerosis of the intrinsic gastroduodenal arteries in abetting the ulcer diathesis. Case summaries of the thirteen patients dying of coronary occlusion and exhibiting peptic ulceration at necropsy are presented from a consecutive series of 168 cases of fatal coronary occlusion; this represents an incidence of peptic ulceration in this group of 7.7 per cent. Case summaries of five patients, dying of hypertensive heart disease and exhibiting peptic ulceration at necropsy, are also presented; these were culled from a consecutive series of 116 patients dying of hypertensive heart disease, an incidence of peptic ulceration in this group of 4.3 per cent. Of additional note, fourteen patients (12.1 per cent) in this group revealed a gastric mucosa described as inflamed, congested, or hemorrhagic.

4. The pathogenesis of fat embolism attending fracture is reviewed, emphasizing the etiological significance of fat emboli in the experimental production of gastroduodenal ulceration. Case summaries of eight patients with fractures of long bones who, at necropsy, exhibited acute peptic ulceration are presented; these were collected from a series of 375 autopsies of patients dying with long bone fractures, an incidence of 2.16 per cent.

5. The etiological factors, common to both chronic ulcerative colitis and peptic ulcer, are briefly reviewed. Case summaries of four patients with chronic ulcerative colitis who, at necropsy, exhibited concomitant gastric and/or duodenal ulceration are presented; these were collected from a series of ninety-one autopsies of patients dying of chronic ulcerative colitis, an incidence of 4.3 per cent.

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OBSERVATIONS ON THE PREPARATION OF HYPERTHYROID PATIENTS FOR SUBTOTAL THYROIDECTOMY WITH PROPYLTHIOURACIL

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A MONUMENTAL work was published by William Stewart Halsted in 1920 in The Johns Hopkins Hospital Reports. With painstaking exactness and unprecedented completeness, Dr. Halsted set forth *The Operative Story of Goitre*[1] and added the details of his own operative technique for goiter (Fig. 1). No more lucid account of the surgical history of goiter has since appeared, and no more than minor alterations have modified the fundamental techniques Dr. Halsted devised in his own operation.

Yet, advances in the surgery of the thyroid gland have been forthcoming. The advent, in the year of Dr. Halsted's death, of iodine therapy for hyperthyroidism[2] permits preoperative amelioration of the disease, and this treatment, by producing involution of the hyperplastic gland, has made the technical aspects of excision easier. The recognition by MacCallum and Voegtlin[3] that the tetany induced by parathyroidectomy could be abolished by administration of calcium has rendered this occasional complication of goiter operations less fearsome. The isolation[4] and the identification[5] of the thyroid hormone have allowed the development of a satisfactory treatment for hypothyroidism resulting from removal of too much thyroid tissue. The determination of the basal metabolic rate,[6] the measurement of serum protein-bound iodine as a reflection of the amount of circulating thyroid hormone[7] and the use of minuscule quantities of radioiodine as a tracer to assess the thyroid's avidity for iodine[8, 9] have provided adjunctive tests in ascertaining the presence and severity of thyrotoxicosis. The studies of thyroid histology by Goetsch[10] and of thyroid anatomy by Rienhoff[11] have afforded knowledge of fundamental importance to both surgeon and clinician. The anesthetist's improved skill in using constantly improving anesthetics, the introduction of tracheal intubation during thyroidectomy, and the advent of antibacterial medications have led toward making the once formidable procedure of thyroidectomy now one of only slightly more than routine interest.

As Dr. Halsted recognized, the goiter operation commanding greatest respect was that for "toxic" goiter. The mortality of this operation in Halsted's day was variously reported as from 3 to 12 per cent.[1] Indeed, even with the advances mentioned, the mortality remained at about 0.5 to 2 per cent.[12, 13] The advent and application of thiourea and related drugs which induce, at least

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during exhibition, subsidence of the hypermetabolic manifestations of hyperthyroidism have further reduced the surgical mortality of subtotal thyroidectomy of toxic goiter to less than 0.23 per cent.[14]

During the six-year period from 1946 through 1951, 729 goiter operations were performed at The Johns Hopkins Hospital. One hundred sixty-one of these were for toxic goiter. Propylthiouracil was used preoperatively in 111 patients.* The data reported herein were collected from a review of the records of these patients, many of whom the author personally has treated, and they are concerned chiefly with observations on the efficacy of propylthiouracil as a preoperative medication in hyperthyroidism.

THYROIDECTOMY

> "If a surgeon should be so adventurous or foolhardy as to undertake the enterprise,† I shall not envy him his feelings while engaged in the performance of it, or after he has completed it, should he be so fortunate as to do this. Every step he takes will be environed with difficulty, every stroke of his knife will be followed by a torrent of blood, . . . No honest and sensible surgeon, it seems to me, would ever engage in it." (Gross, 1886.[1])

THE OPERATIVE STORY OF GOITRE

THE AUTHOR'S OPERATION

By WILLIAM S. HALSTED, Baltimore, Md.

The extirpation of the thyroid gland for goitre typifies, perhaps better than any operation, the supreme triumph of the surgeon's art. A feat which today can be accomplished by any really competent operator without danger of mishap and which was conceived more than one thousand years ago might appear an unlikely competitor for a place in surgery so exalted.

Fig. 1.—First paragraph of monograph, *The Operative Story of Goitre,* by William S. Halsted.

A classification of the 729 thyroid operations is recorded in Table I. The extent of the operative procedures varied widely. In some instances only a biopsy of the gland was performed whereas in some cases, huge goiters with intrathoracic extension were removed. Extensive dissection of the neck for carcinoma of the thyroid was performed in several instances. While several patients have died since operation from causes unrelated to the thyroid disease or from advancing carcinoma of the thyroid, no patient died during thyroidectomy. One patient died in the immediate postoperative period: a 48-year-old woman was found dead in bed forty-eight hours after the facile removal of a moderate-sized, nontoxic goiter; at autopsy, slight aspiration pneumonia was noted. Thus, in this series there was a mortality incidence of 0.14 per cent. No fatality occurred among the hyperthyroid patients.

Table II lists the types of preoperative management employed in the 161 patients undergoing subtotal thyroidectomy for toxic goiter. Thiouracil, used in 19 patients, was discontinued in May, 1946, in favor of the less toxic, equally

*A portion of the propylthiouracil (6–n–propyl–2–thiouracil) used in this study was kindly supplied by Dr. Stanton M. Hardy of the Lederle Laboratories, Pearl River, N. Y.

†That is, extirpation of goiter.

TABLE I. DISTRIBUTION OF 729 THYROID OPERATIONS PERFORMED FROM 1946 THROUGH 1951

YEAR	NUMBER AND TYPE OF OPERATION					
	NONTOXIC GOITER*	TOXIC GOITER	CARCINOMA	THYROIDITIS†	BIOPSY‡	TOTAL
1946	93	49	9	2	1	154
1947	56	27	14	4		101
1948	76	17	12	2		107
1949	82	17	9	5	1	114
1950	90	26	7	5	1	129
1951	83	25	11	6		125
Total	480	161	62	24	3	730§

*In this group of patients there were instances in which the diagnosis clinically, and later pathologically, was that of nontoxic goiter yet, because the clinical diagnosis was in some question, preoperative medication was given as a precautionary measure. Five patients received iodine therapy, 3 received thiouracil and iodine, 1 received only thiouracil, and 4 received propylthiouracil and iodine. In addition, one patient had received propylthiouracil for a short period about six months before operation and another, five years before operation.

†Includes giant-cell type, struma lymphomatosa, Riedel's struma, and Letterer-Siwe disease.

‡One patient was receiving propylthiouracil when biopsy was performed.

§Although only 729 operations were performed, the total is listed as 730, since 1 patient operated upon in 1947 had both toxic goiter and carcinoma of thyroid.

efficacious, propylthiouracil. While the duration of preoperative propylthiouracil therapy varied widely, the administration of the drug, with only a few exceptions, was continued through the day immediately prior to the operation. Iodine, usually as Lugol's solution, was also administered to the majority of patients receiving propylthiouracil; duration of this therapy was also variable, however, only infrequently being less than ten days of the immediate preoperative period. In 4 patients propylthiouracil alone was used; 2 of these patients had previously demonstrated sensitivity reactions to iodine and, in 2, iodine was intentionally withheld in order to observe the histologic change in the goiter occurring with propylthiouracil therapy only. The more recently developed drug, methimazole,* was used along with iodine in 2 patients in 1951, and is now receiving further study.

TABLE II. TYPES OF MEDICATION USED IN PREPARATION OF 161 HYPERTHYROID PATIENTS FOR SUBTOTAL THYROIDECTOMY

YEAR	NUMBER OF PATIENTS						
	THIOURACIL AND IODINE	PROPYLTHIOURACIL AND IODINE	PROPYLTHIOURACIL ONLY	IODINE ONLY	METHIMAZOLE AND IODINE	NO TREATMENT	TOTAL
1946	18	13		17		1	49
1947	1	23	1	2			27
1948		15		1		1	17
1949		14	1	2			17
1950		22		4			26
1951		20	2	1	2		25
Total	19	107	4	27	2	2	161

PREOPERATIVE PROPYLTHIOURACIL THERAPY

Astwood's[15] introduction of thiourea and thiouracil therapy was appreciated almost immediately by clinicians and surgeons as a means of gaining control of thyrotoxicosis before submitting a hyperthyroid patient to subtotal thyroidectomy. At first, it appeared that these agents increased the vascularity of the

*Furnished by Dr. D. C. Hines, Eli Lilly & Co., Indianapolis, Ind.

thyroid gland, thus increasing the likelihood of hemorrhage during, or immediately after, operation. Later, the recognition that these drugs require several weeks of administration to exert full therapeutic effect and, further, that with prolonged therapy vascularity of the gland is usually not increased led to their application in nearly every case in which the extent of the hypermetabolism gave jeopardy to the operation. When thiouracil was found to produce agranulocytosis in an incidence sufficient to make its widespread use injudicious, propylthiouracil, a similarly acting and less hazardous drug, was introduced.

The experience gained in this hospital in 1944 with thiouracil[16] indicated that a period of therapy of approximately one month was necessary before significant reduction in the rate of metabolism was obtained. In 1946, when propylthiouracil was first available, a short period of preoperative therapy was employed because the ideal dose and toxicity of the drug were not known. Since establishment of the drug's efficacy and safety, a course of therapy of sufficient duration to bring well-defined amelioration of the disease prior to subtotal thyroidectomy has been established and followed whenever practicable. Table III shows the duration of propylthiouracil therapy prior to operation; the tendency toward a more prolonged period of preoperative treatment in recent years is apparent.

TABLE III. DURATION OF PREOPERATIVE PROPYLTHIOURACIL THERAPY IN 111 PATIENTS WITH HYPERTHYROIDISM

YEAR	LESS THAN 2 WEEKS	2 TO 4 WEEKS	4 TO 8 WEEKS	8 WEEKS TO 3 MONTHS	3 TO 6 MONTHS	6 TO 12 MONTHS	OVER 12 MONTHS
1946	1	4	4	4			
1947	2	5	9	6		1	1
1948		1	5	4	3	1	1
1949		4		2	3	6	
1950		2	2	3	8	5	2
1951			2	5	4	5	6
Total	3	16	22	24	18	18	10

Evidence exists to suggest that the basal metabolic rate should not be used as the sole criterion for determination of the existence of euthyroidism during treatment. In some instances, the basal metabolism has returned to normal ranges after twenty to thirty days of therapy yet, when adjudged by other means, the patient has not attained euthyroid status. With continued therapy, the patient may continue to gain previously lost weight and recover slowly the composure of person that existed prior to the onset of the disease.[17] To allow this period of physical and emotional readjustment to occur has, in the experience of the members of this hospital, permitted an ease in handling the patient and in operative performance not heretofore known. Further, the attainment of complete euthyroidism preoperatively allows an election of the time of operation most suitable to the patient, the surgeon, and the hospital.

OPERATIVE PROCEDURE

In only four instances of the propylthiouracil-treated patients did the surgeon mention that vascularity of the thyroid made excision difficult. Occasionally, however, especially in patients treated one month or less, marked

vascularity was noted and considerable effort to secure hemostasis was necessary. In general, those patients who had received propylthiouracil for three months or longer, with Lugol's solution added at least seven days before operation, had glands which posed no special problem to the surgeon; indeed, in some the excision of the gland was compared to the removal of a nontoxic goiter.

Similarly, friability of the thyroid gland was seldom encountered. An exception occurred in a 35-year-old woman who received two courses of propylthiouracil. The first was of fourteen months' duration and was followed by a recurrence of hyperthyroidism within five months. Propylthiouracil, 200 mg. daily, was then administered for fifteen months. For two weeks prior to operation she had received Lugol's solution in addition to propylthiouracil. At operation marked friability with slight increase in vascularity of the gland made excision difficult.

Anesthesia in the propylthiouracil-treated patients was carried out without difficulty except in rare instances. After a study of the anesthesia charts, it seems fair to conclude that, in general, anesthesia was accomplished with greater facility in those patients with well-established euthyroidism than in those with only partially controlled hyperthyroidism. Furthermore, in the euthyroid patients under good anesthesia the surgeon was allowed time for effective hemostasis and careful identification of anatomic structures.

It is also of interest that no two-stage operations were required during this six-year period, and that transfusions were only rarely necessary.

CONVALESCENCE

> "... the patient left the hospital perfectly recovered on the 34th day after the operation." (Desault reported by Giraud, 1792.)
>
> "... on the 21st day after the operation the patient left for her home in the country." (Cooper, 1862.)
>
> "... in about 12 days the patient's condition was quite normal." (Sick, 1867.[1])

Propylthiouracil has permitted a decrease in the period of hospitalization formerly considered as necessary for preparation for and convalescence from subtotal thyroidectomy. In nearly every patient who had been adequately prepared on an outpatient basis, the operation was performed on the day after the patient's admission to the hospital. Moreover, the preoperative use of propylthiouracil appears to have lessened the period of hospitalization required postoperatively. The hospital convalescence was as brief as four days for a few patients, some of whom had had severe hyperthyroidism prior to the initiation of propylthiouracil therapy.

Furthermore, a study of those patients whose discharge from the hospital was not delayed for reasons other than the operation or its complications gives evidence that convalescence may be more rapid in those who receive propylthiouracil for a period sufficient to permit the attainment of distinct euthyroidism. Twenty-three (37 per cent) of 62 patients treated with propylthiouracil for less than three months required more than ten days in the hospital postoperatively, whereas only 7 (16 per cent) of 43 patients who received propylthiouracil three months or longer required more than ten days.

COMPLICATIONS OF OPERATION

A comparison of the complications of subtotal thyroidectomy during the past six years with those of any other period is not practicable. The introduction of improved anesthesia, antibiotic therapy, and so forth, would render such a comparison valueless. However, a brief accounting of the complications encountered and their incidence may be of value; these are not dissimilar to those reported by Cattell.[18]

HYPOPARATHYROIDISM

> "A few days after the operation the patient surprised those around her by her singularly restless and dissatisfied demeanor; she complained continually of sleeplessness. . . . On the evening of the sixth day the patient was seized with convulsions of the extremities, without losing consciousness . . . the patient had a second attack, . . . and a third; but these last were much milder than the first attack. . . . There remained . . . the asseveration of the patient that before the operation she had never suffered from such attacks, and also the circumstance that during the subsequent four weeks of her stay in the hospital she was quiet and contented, that the attacks were not repeated and that sleep returned." (Wölber writing of Billroth's first case of tetany, 1879.[1])

During the postoperative period, 9 of the 111 patients had manifestations of hypoparathyroidism. This was usually manifest by the elicitation of positive Chvostek and Trousseau signs. Severe tetany was not encountered, probably because of the early institution of calcium therapy. Only 1 patient developed permanent hypoparathyroidism. In only 1 of the 9 patients was parathyroid tissue found in the operative specimen.

It is of interest to note that in 3 patients the surgical pathologist found a parathyroid gland in the operative specimen. Yet these patients developed no manifestations of hypoparathyroidism postoperatively.

INJURY TO RECURRENT LARYNGEAL NERVES

> "A young man had a goitre the size of an apple removed. During the operation he suddenly became speechless; . . . The loss of voice lasted for three weeks; by degrees the patient began to speak again." (Klein quoted by Wöfler, 1818.[1])

This complication occurred in 5 patients, being unilateral in 4 and bilateral in one. Insufficient follow-up data were available to determine if these were permanent.

POSTOPERATIVE HYPOTHYROIDISM

> "Two or three months after the operation* the patients have, for the most part, presented a state of feebleness, pallor, anemia, accompanied . . . with edema of the face and hands, without albuminuria." (Revendin, 1882.[1])

Myxedema subsequent to the operation is known to have occurred in 4 patients. There are insufficient follow-up data available to allow conclusions regarding the incidence of this complication.

*That is, total ablation of goiter.

POSTOPERATIVE "STORM"

An exacerbation of hyperthyroidism manifested by marked agitation, fever, and inordinate tachycardia occurred in 6 patients during the immediate postoperative period. Five of these patients had received both propylthiouracil and Lugol's solution for three weeks or less, and the sixth patient had been treated for four weeks. While in each instance amelioration of the disease had been apparent during treatment, the extent of the improvement was not striking. These, indeed, were instances of mild to moderate postoperative "storm," and nothing comparable was observed in the patients more extensively treated preoperatively with propylthiouracil. These experiences focus attention on still another advantage of securing well-defined euthyroidism prior to subtotal thyroidectomy.

TABLE IV. COMPLICATIONS OF SUBTOTAL THYROIDECTOMY IN 111 HYPERTHYROID PATIENTS PREPARED FOR OPERATION WITH PROPYLTHIOURACIL

TYPE OF COMPLICATION	NUMBER OF PATIENTS
Hypoparathyroidism	9
Injury, recurrent laryngeal nerve	6
Hypothroidism	4
Infection	1
Hematoma	10
Postoperative storm	6

OTHER ASPECTS OF THERAPY

By virtue of propylthiouracil's effectiveness in ameliorating thyrotoxicosis, subtotal thyroidectomy was accomplished in several patients in whom the operation otherwise would have been impossible. Auricular fibrillation, the complication of hyperthyroidism which Dr. Halsted stated increased greatly the hazard of operation, disappeared during the induction of euthyroidism by propylthiouracil in 3 patients; the eventual operations were uneventful. Two patients had severe cardiac failure when first seen; after several months of treatment with propylthiouracil all manifestations of cardiac insufficiency regressed and operation was permitted. Six patients had moderately severe diabetes mellitus, 4 patients had hypertension, 1 had right bundle branch block, and 1 had bronchiectasis; in each, subtotal thyroidectomy was performed without untoward event. It was also of interest that a patient with psychosis and Graves' disease had the hyperthyroidism well controlled before subtotal thyroidectomy was performed; in this patient operation appeared injudicious during active hyperthyroidism for fear of an exacerbation of the psychotic state.

In the group of propylthiouracil-treated patients, the youngest operated upon was 16 years of age and the oldest, 68 years of age. It was of interest that 15 patients were over 60 years of age at the time of operation.

Among the patients prepared for operation with Lugol's solution were 2 who had previously demonstrated sensitivity reactions to propylthiouracil. Each of these patients developed urticaria fourteen days after the initiation of therapy with propylthiouracil; one of these has been reported.[17] Another patient developed severe pruritus due to propylthiouracil and was prepared for operation by the administration of methimazole and Lugol's solution.

CONCLUSIONS

The preoperative amelioration of the hypermetabolic manifestations of thyrotoxicosis can be obtained by the administration of propylthiouracil. Since hyperthyroidism responds slowly to the drug, the duration of preoperative administration should not be less than three months. The attainment of a completely euthyroid state allows an election of the time of the operation, the removal of any fear on the part of the patient concerning the operation, easy induction and maintenance of the anesthesia, an unhurried facility of operative procedure, and a shortened convalescence. The likelihood of postoperative exacerbation of hyperthyroidism is almost entirely removed. From the experience gained in The Johns Hopkins Hospital during the past six years, it appears that a preoperative course of propylthiouracil is advisable in all patients with moderate to severe hyperthyroidism. Lugol's solution is usually administered concomitantly with propylthiouracil during the two weeks prior to operation. There has been no operative mortality in 111 cases prepared for operation with propylthiouracil, and the morbidity of the operative procedure also appears minimal. The preoperative use of propylthiouracil, or a similarly acting drug, has now become a well-standardized procedure and occupies a secure position in the armamentarium of the clinician and surgeon in the treatment of this disease.

Dr. Halsted's monograph, *The Operative Story of Goitre,* was one of his greatest works and was published only two years before his death. His conclusion, modest of his own role in the development of thyroidectomy and seemingly prophetic of his approaching demise, states, "And now, . . . in the brief span of one life, surgery, so it seems, has marched from the beginning to near the end of its great era—the great era of operative development." We, his students avidly following his precepts, have seen the more difficult operation of excision of toxic goiter become simplified by means of preoperative control of hyperthyroidism.

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ADRENALECTOMY FOR HYPERTENSION

Advantages of the Anterior Abdominal Approach

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RECENT interest in bilateral adrenalectomy has been aroused for the treatment of certain selected hypertensive patients. The failure of sympathectomy (regardless of the extensiveness of the resection) to reduce the blood pressure in a respectable number of cases naturally steers the surgeon into other procedures which may reduce the pressure. Sympathectomy permits alleviation of some of the hypertensive symptoms even though the pressures remain at a hypertensive level. Nevertheless, a surgical attack upon this disease should include a reduction of the blood pressure as well as alleviate symptoms, if it is to establish itself materially as a sound method of therapy. It is to be noted that institutions differ in their attitude depending upon the demand placed upon them for therapy. Clinical material varies and consequently when the institution is called upon to treat hypertensive patients in the late stages when organic lesions are seriously manifested, often beyond the extent suitable for safe sympathectomy, an attack upon the adrenals may be desirable.

Hypertensive patients drifting into Kennedy Hospital are usually of two types—the malignant hypertensive where the elevation of the blood pressure rises to a critical level in a short period of time or the chronic case handled by the family physician and his specialists until the organic changes are such that death is expected as the patient enters a terminal state. We seldom see the labile type or the early essential hypertensive case. These few are treated medically with apparent success for long periods of time. Perusal of the monthly death list reveals a strikingly large number of cardiac deaths where hypertension has been the sole contributor to the cardiac disease.

Prior to June, 1951, sympathectomy was employed with a mortality rate of approximately 19 per cent and a pressure reducer rate of only 8 per cent. This discouraging experience is undoubtedly modified by the attempt to employ sympathectomy in patients too ill to stand the procedure. Reducing drugs have thus far not been too satisfactory, although the use of Hexamethonium and Apresoline appears to be more encouraging.

Adrenalectomy was employed for hypertension by DeCourcey[2] in the late twenties and early thirties. The mortality rate was very high if small amounts of adrenal tissue remained, and the course of the disease was not materially altered if large amounts of adrenal tissue remained. Enthusiasm for bilateral adrenalectomy waned until better substitutive drugs were available. Cortisone, DCA, aqueous extract, and fatty extract of the adrenal, when used in proper

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proportions, have made adrenal surgery much safer in the hypertensive patient as well as the hormone-producing tumor patients. Green and associates[3] and later Zintel and his co-workers[6] employed partial adrenalectomy with some degree of success in selected far-advanced cases. One is immediately aware of the fact that the types of cases selected by these workers are the types which present a great problem to a Veterans Administration hospital and we set up a protocol for the study of the benefits that may be derived from adrenalectomy in severe hypertension. Medical department cooperation has been obtained, and the cases are selected by the cardiologist, who insists upon the following:

1. Uncontrollable malignant hypertension.

2. Chronic hypertensive cases when the organic changes are unquestioned, and after thorough study a prognosis of death in the near future (one year) is anticipated. No one can be so accurate about the prognosis as just stated, but the cardiologist must be convinced of the vulnerability of the organic findings before he will suggest adrenal surgery. According to the usual custom of medical consultants, the patients are very ill and the mistakes, if any, are made on the side of waiting longer in order to establish the criteria of nonrecovery. In other words, none but the desperately ill patients are sent for surgery.

The four systems, the brain, blood vessels, heart, and kidneys, are studied and the findings recorded in terms of 1 plus to 4 plus. The various combination contraindicators which judge the sympathectomy possibilities are not employed. All cases show organic changes in all four systems, although variation of intensity of involvement exists. Encephalopathy with cerebral accidents, large, multiple, or otherwise, do not contraindicate. Two of the patients blinded completely by choked disc and hemorrhages demonstrate the fact that these do not cause denial of operation. Cardiac decompensative episodes and coronary disease do not necessarily prevent operation unless the cardiac condition is so near a terminal one that temporary improvement is not possible. Poor kidney function appears to be the real contraindicator. Urea clearance test has been significant. We have already learned that a clearance below 50 per cent is a dangerous one from an operative standpoint. Our third patient, the first death, had a urea clearance of 22 per cent and died of uremia thirteen days after the first left-sided adrenalectomy. The fourth death accompanied a urea clearance of 32 per cent. Experience with the organic lesions, and the studies of them, is aiding materially in the development of medical and surgical judgment of the cases.

The operative attack then calls for planning, first the selection of the case for surgery; second, the pre- and postoperative specific therapy; third, the surgical technical problems, and fourth, postoperative and maintenance problems.

Operation.—We decided to perform a two-stage adrenalectomy, leaving a small piece of live adrenal tissue on the left side and removing the entire right adrenal. The retained adrenal was assigned to the left gland because the best blood supply seemed to exist in the left lower pole where the artery and vein from the renal vessels seemed to us to be constant, and the vessels of some size. The remnant ranges from the size of the nail of the little finger to that of the thumbnail. Exact measurement of the remnant of course is desired, but the fat

surrounding the remnant must not be disturbed if one is to be sure that the blood supply has not been compromised, and therefore sight and touch are relied upon for this estimation.

Adrenalectomy can be done by the lumbar, abdominal, or thoracolumbar incisions. One recognizes that the operator usually and sensibly employs the approach most familiar to him. Any one of the three approaches will permit removal of the entire gland, but the saving of a small viable remnant appears difficult in the lumbar approach, and the thoracoabdominal approach is not necessary to gain this viability. The adrenal glands are located anterior and medial to the upper pole of the kidney. In this respect they are not entirely posterior structures. Cahill,[1] the urologist, has championed the abdominal approach. Zintel,[6] Priestley,[5] and Green[3] prefer the posterior approach. The abdominal approach permits palpation of both adrenals via one incision, so that the operator knows whether or not tumefaction exists in either gland, before any adrenal tissue is removed.

Left Side.—Subcostal incision is from midline to anterior axillary line. After peritoneum is opened, palpation of the right adrenal rules out neoplasm of that gland. This can be done with extreme accuracy. The right adrenal usually rests behind and slightly lateral to the vena cava. One locates the upper pole of the right kidney and sweeps the hand from it to and behind the vena cava. If there is no tumor on the right, the operator prepares for the exposure of the left adrenal. There are two methods:

1. Gastrocolic omentum is divided and vessels are ligated. Retractors are placed reflecting the stomach toward the xiphoid process, the transverse colon downward, and the outer gastrocolic omentum and spleen laterally (Fig. 1). The upper edge of the pancreas and splenic artery are located, and with the hand they are retracted downward. Incision of the thin posterior peritoneum reveals the adrenal gland resting in the perirenal fat. Lateral and medial edges are dissected free gently and the tissues at the upper pole separated. A moderate-sized vessel at the upper pole is inconstantly seen. By grasping perirenal fat and gently pulling, the adrenal is elevated from the depth of the incision. Now one can see the two large vessels along the medial and lower pole of the adrenal. Clamp or clamps are applied in a fashion to leave the desired amount. Careful ligation or transfixion of the vessels is done. Inspection now verifies size of remnant and adequacy of blood supply. The gland is always in view of the operator who can accurately know the size of remnant. If the gland is torn during manipulation, the operator can expose and remove the desired adrenal tissue with ease. Most of the glands are removed without tearing, which is preferable.

2. This method entails separation of the gastrohepatic peritoneum, ligation of the left gastric vessels, and retraction of the left lobe of the liver upward and the stomach downward and laterally. This approach is quite simple in thin patients. The pancreatic edge is located, retracted downward, peritoneum incised, and the adrenal comes into view. However, this exposure has been employed in only two cases.

Comments.—Two early cases caused difficulty. The gastrocolic omentum was incised to the vasa brevia and the retractor tore a capsule of spleen, requiring splenectomy. The patient died of uremia (see deaths) thirteen days postoperatively, but operative technical difficulty was believed not to be responsible. The operation required two hours and one blood transfusion.

The second patient was a 235 pound, five-foot two-inch Negro. The tail of the pancreas coursed directly upward instead of laterally. Resting in the fat, the tail of the pancreas was mistaken by the operator for the adrenal. The adrenal was finally located and successfully removed, but the splenic artery had been injured and splenectomy was necessary. The patient recovered. Operation required one hour, fifty minutes and two blood transfusions.

The operation is easy for an operator familiar with the region and accustomed to pancreatic surgery. It requires no manipulation or displacement of the kidney. In fact, the kidney is not always seen but can be felt. It requires no rough manipulation, nor is it as extensive as the lumbar rib-removing operation. None of the painful episodes sometimes observed in the lumbar approach has been observed. Occasionally one observes hypotension or normal tension after this stage, but it is unusual and can be handled readily with Neosynephrine and glucose intravenously. Blood transfusion postoperatively was used in one hypotensive patient with excellent response.

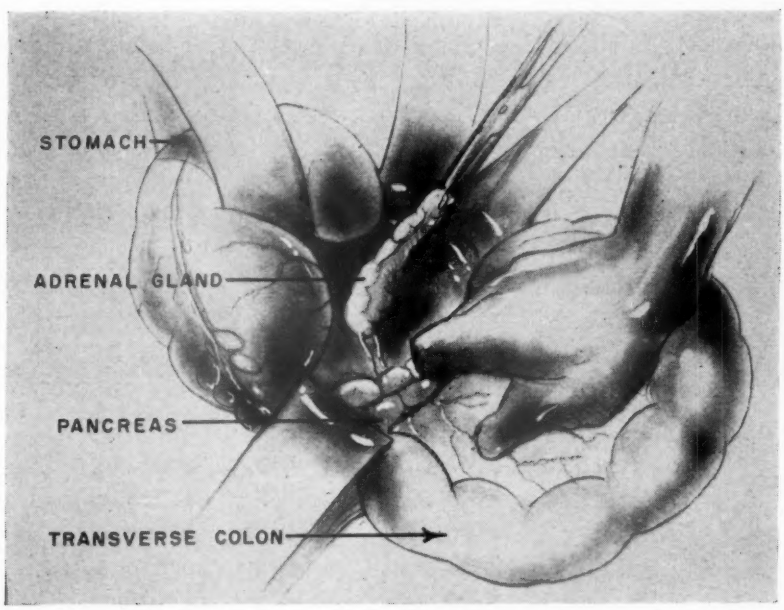

Fig. 1.—Exposure for left partial adrenalectomy.

It is to be noted that in the first two cases, the remnant blood supply was questionable. Subsequent management suggests that one of these patients may be totally adrenalectomized, but all others require so little cortisone therapy that one can be certain of the viability of the remaining tissue. A Levin tube is inserted the morning of operation for gastric decompression and is allowed to remain from twenty-four to forty-eight hours postoperatively. Discounting

the two cases noted, these patients recover promptly with less trouble than in the average cholecystectomy case. The procedure requires from forty-five minutes to one hour with slow gentle operating in the average case. A cigarette drain is placed to the site of removal. Minor injury to the tail of the pancreas existed in two cases, but no serious pancreatic manifestations were observed. No pancreatic fistula has occurred. It is to be noted that a few deaths[5] have been reported where necrosis of the pancreas was found at necropsy. One may conjecture that the operators, working through a posterior incision, did not realize possible injury to the pancreas and did not drain the injured pancreas, and pancreatic necrosis developed. If this is true, the anterior approach should add to the safety of the operation.

Interval.—The time between stages necessarily varies according to the condition of the patients. One totally blind, malignant hypertensive patient underwent the second stage five days after the first, while still convulsing from encephalopathy. The average interval however is two to four weeks. One patient remained at normal pressure level for three months and was not subjected to the second stage until the pressure resumed its hypertensive level. With better understanding of the disease, the operation and postoperative care, it may be possible to perform safely both sides in one stage. This has been safely and easily done in prostatic malignancy with metastasis.

Preoperative Therapy.—The preoperative therapy is rather simple and for the sake of brevity is about the same as that outlined for bilateral adrenalectomy by Huggins and Scott.[4] Ostensibly, it means a twenty-four or forty-eight hour preoperative period with 50 mg. cortisone twice daily, and 5 mg. of DCA the morning of operation. In our early cases the twenty-four hour plan was used (100 mg. cortisone and 5 mg. of DCA), but recently we have used the forty-four hour method (300 mg. cortisone and 5 mg. DCA). The change was effected because there seemed to be a delay in the cortisone action in the twenty-four hour plan which caused great concern and forced the use of Neosynephrine and blood transfusions for a period of hours until the cortisone could maintain elevated pressure. The plan to be described here has proved to be very safe. The postoperative course of the last six cases has been entirely uneventful.

For operation Monday, 8:00 A.M.

Saturday	12:00 Noon	50 mg. cortisone
Saturday	8:00 P.M.	50 mg. cortisone
Sunday	10:00 A.M.	50 mg. cortisone
Sunday	2:00 P.M.	50 mg. cortisone
Sunday	6:00 P.M.	50 mg. cortisone
Monday	6:00 A.M.	5 mg. DCA
Monday	7:30 A.M.	50 mg. cortisone

Right Side.—Right subcostal incision is made. The right lobe of the liver is retracted upward and laterally. The hepatic flexure is retracted downward and the duodenohepatic peritoneum is incised. The duodenum is mobilized and retracted medially. The vena cava is located and freed of areolar attachments and retracted medially. The adrenal comes into view (Fig. 2) and often rests entirely behind the vena cava, but exposure is gained with ease. The lower pole

and medial and lateral edges are freed by sharp and blunt dissection. Small vessels are clipped or clamped and ligated. At the upper pole one sees a moderate-sized vein which enters the vena cava. After this vein is clipped the gland is removed. We have observed very few blood vessels supplying the right adrenal. Gelfoam is placed in the fossa. A cigarette drain is inserted, and the incision closed in the usual manner.

Comments.—Right total adrenalectomy is a very easy operation with the abdominal approach. Difficulty has been encountered in one case when the retractor reflecting the vena cava tore a small hole in the renal vein. This was sutured promptly and without the loss of more than 100 c.c. of blood. The accident was due to marked arteriosclerosis in the renal artery to which the vein was attached by adhesions. The vein gave with the pull, the sclerotic artery would not yield, and the tear resulted. All patients, even the obese ones, have not required more than one hour's operating time. As an operating procedure, patients have recovered from the second stage with less trouble than the left side.

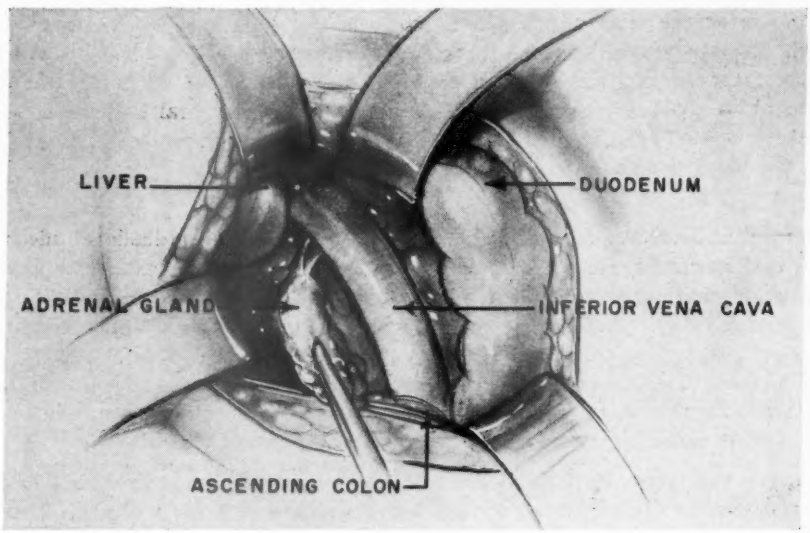

Fig. 2.—Exposure for right total adrenalectomy.

The postoperative patients must be closely observed and prompt changes in therapy instituted if serious drops in pressure follow.

The postoperative plan consists of 50 mg. cortisone, q.6h., intravenous glucose in salt, and blood transfusions if necessary. Neosynephrine and aqueous adrenal extract are sometimes temporarily employed. When serious hypotension does not linger, smaller doses of cortisone are given and the drug is gradually reduced until the pressure is normal level, and no serious signs of hypo-adrenalism exist. Reduction of the cortisone dose begins around the forty-eighth hour in the average case, and is completed in around two weeks. Maintenance dose varies from 25 mg. daily in a few cases to no cortisone in two cases. One case requires 50 mg. daily. A few patients take it every second day, and one every third day. Obviously, the maintenance dose varies with each patient and is regulated by the height of the pressure and the degree of hypoadrenalism.

Patients on maintenance must be closely observed and have access to hospitalization if hypoadrenal crisis appears. Ordinary infections such as upper respiratory infections are dangerous and will induce crisis, because of the inability of the hypoadrenal patient to combat infection. DCA is helpful during a crisis. The crises are alarming, but have not been the cause of death in any patients. The episodes are short-lived. Crisis therapy, however, cannot be delayed long without fatality.

DEATHS

CASE 1.—A 39-year-old patient had malignant hypertension with urea clearance of 22 per cent, 1 plus eye ground changes, 2 plus cardiac. Splenectomy was required because of retractor injury to the spleen. Blood transfusions were given. The patient remained oliguric and died of uremia on the thirteenth postoperative day.

CASE 2.—A 34-year-old patient had malignant hypertension with systolic pressures often higher than manometer could record. Diastolic pressure averaged 160 mg. Hg. The patient underwent twenty-one operations during World War II for abdominal actinomycosis, and nearly died from hemorrhage each time from a blood dyscrasia termed "capillary fragility." The patient was restless and suffered terrifying headaches. Medical consultants did not have Hexamethonium at the time and urged adrenalectomy. The surgeon hesitated, but finally capitulated. A left partial adrenalectomy was performed without incident and with very little oozing. However, the patient bled from the wound and died forty-eight hours later of hemorrhage which could not be controlled. Autopsy showed cerebral edema, cardiac enlargement, enlarged spleen, small contracted kidneys, and intraperitoneal hemorrhage. The exact nature of the blood dyscrasia was undetermined.

CASE 3.—A 64-year-old patient had chronic hypertension with encephalopathy 3 plus, vessels 3 plus, cardiac 3 plus, and kidney 2 plus. Also chronic duodenal ulcer. Massive gastrointestinal hemorrhage occurred five days after left partial adrenalectomy and necessitated emergent gastric resection with prompt recovery. The patient died thirty-two days after the second stage. Autopsy revealed focal necroses in the brain, particularly in the medulla, suppurative pericarditis, and small contracted kidneys. This patient's blood pressure was reduced to a lower level—preoperative 230/140, postoperative 180/110—but was not reduced to normal tension. So far, this is the only case where the pressure has not dropped to normal, and is classified as a failure. The adrenal remnant was viable.

CASE 4.—A 41-year-old patient had malignant hypertension with several cerebral accidents, encephalopathy 4 plus, vessels 3 plus, heart 2 plus, and kidneys 3 plus. Urea clearance of 32 per cent was elevated to 48 per cent after one month of rice diet therapy. The patient died suddenly the night of the second stage operation with convulsions and respiratory cessation. Adrenal insufficiency was not believed to be the significant cause of death. Autopsy showed focal necroses in the brain, old cerebral hemorrhage, arteriosclerosis, enlarged heart, small contracted kidneys, and several large blood clots in the operative area. Death was due to cerebral involvement. The blood supply of the remnant was good.

CASE 5.—A 39-year-old white man with malignant hypertension 240/140, marked encephalopathy, vessels 3 plus, brain 4 plus, kidneys 1 plus, and heart 1 plus, demonstrated vomiting, convulsions, and Jacksonian seizures. Hexamethonium bromide dropped the pressure slightly, but induced marked paralytic ileus and its use was abandoned. Twelve days after left partial adrenalectomy, the patient died with generalized convulsions and cessation of respiration. Autopsy revealed subacute glomerular nephritis, cerebellar edema with encephalomalacia, infarction kidney, cardiac hypertrophy, and congestion of lungs, liver, spleen, and kidneys.

SUMMARY AND CONCLUSIONS

At the time of this writing, twenty-three patients have been subjected to operation. Four deaths occurred in ultra desperate cases in patients subjected

to operation in the days of early experience. These deaths are directly described as postoperative deaths. The fifth death occurred approximately two months postoperatively. There has been only one instance of failure to reduce the systolic and diastolic pressures to a normal level. Several patients require enough cortisone to elevate the systolic pressure slightly (160 to 170 mg. Hg.), but if the cortisone dose is lessened, the pressure falls to a normal or subnormal level. Eighteen cases are presently being followed.

It is not proposed to analyze the results in this paper. Many of the patients have survived more than one year, but the time period is not long enough to report satisfactorily. It is planned to report at the two-year level. Several generalities can be mentioned.

1. Only one patient has failed to return to normal pressure and this same patient has the only death of those surviving bilateral operation.

2. All cases except two require maintenance cortisone therapy ranging from 3 mg. every three days to 25 mg. daily. One case requires 60 mg. daily.

3. Substitutive therapy was not difficult except in the first two cases. It is not expensive—averages about 35 cents per day.

4. Hospitalization and a staff competent to handle Addisonian crisis must be available.

5. Good results are noted in the malignant hypertensive group as well as the chronic case with marked arteriosclerosis.

6. Kidney impairment seems to be the most dangerous preoperative factor. Sodium-free diet has apparently improved the kidney function preoperatively in at least two cases.

7. It is noted that we request the patient to endure a controllable mild hypoadrenal state instead of a fatal hypertensive state.

8. It is realized that this study is in the nature of an investigation and results will be reported in the future regardless of the degree of success or failure.

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THE USE OF AORTIC OCCLUSION IN ABDOMINAL SURGERY WITH A REPORT OF TWO HUMAN CASES

A Preliminary Report

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THERE is at present a tendency to resort to palliative surgical resections when there is a single metastasis to the liver because of the hazards of uncontrollable hemorrhage which may follow attemps at hepatic resection. Hence, patients who might otherwise be salvaged are denied the possibility of cure. For this reason, a study of aortic occlusion as a method which permits certain control of abdominal and hepatic circulation has been undertaken.

The use of aortic occlusion in resections of the liver was chosen for study since it is felt that, if circulation can be controlled in this area of the abdomen, other areas will also yield to this method. Furthermore, if total occlusion of blood supply above the liver is compatible with return of normal function upon restoration of circulation, certainly it should follow that it will be true below this level.

The procedure of high aortic clamping to control blood flow has been applied principally in resections of aneurysms and coarctations. In the course of reviewing the literature, little information was found which applied directly to the use of aortic occlusion in abdominal surgery if aneurysms are excluded. Many of the reports are vague about the time the aorta was occluded in human patients. This is of great importance and must be accurate if this method is to be safely employed.

From a review of the literature it is apparent that during the last thirty years complete aortic occlusion has met with little success. We were unable to find a single case in this thirty-year period in which aortic occlusion has been employed for hemostasis in hepatectomies, although temporary interruptions of the hepatic artery have been employed (Wangensteen[1]). Sporadic experimental studies demonstrate that, within certain time limits, aortic occlusion can be tolerated by dogs.[2-4] Other investigators have deliberately avoided sudden occlusion, and they have partially ligated the aorta over periods of weeks and months in an effort to create collateral circulation, but these studies are not applicable to the use of aortic occlusion in abdominal surgery.

A few cases of complete aortic occlusion in human patients were found in the literature directed toward the treatment of aneurysms by aortic resection. Five cases of complete occlusion of the aorta above the celiac axis were found, and in two of these a satisfactory result was reported. Guinard[5] completely ligated the thoracic aorta for an aneurysm, but the patient died twelve hours

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later of renal insufficiency. Reid[6] ligated the thoracic aorta for an aneurysm, but the patient expired the same day of hemorrhage from an intercostal artery. Andrus[7] doubly ligated and divided the thoracic aorta for an aneurysm of the abdominal aorta, but the patient died one and one-half hours postoperatively from shock. Alexander and Byron[8] reported a successful case of ligation of the thoracic aorta for resection of a thoracic aneurysm. Employing wide cotton tapes, they noted a blood pressure rise to 250/130, followed by a fall to 150/100 after removal of the tapes. Their success was partly due to the extensive collateral circulation. The other successful case was reported by Reid[9] in which he first created a collateral blood supply by partially ligating the abdominal aorta below the renal arteries. Later he was able to occlude the aorta completely just above the celiac axis. The patient died one month postoperatively from a new aneurysm.

In the literature there are thirty cases of ligation of the abdominal aorta below the renal arteries. Of these, only eight were successful in that the ligation was not a cause of death. Of these eight cases, four were complete ligations (Hamann,[10] Matas,[11] Bigger,[12] and Brooks[13]), but there was a partial reestablishment of the lumen in all but the case reported by Brooks; his success was probably due to the abnormal collateral circulation developed prior to the operation. The remaining four cases were deliberately incomplete ligations (Vaughan,[14] Watts,[15] Elkin,[16] and LaRoque[17]).

The problem of resecting aneurysms has become less difficult in the past two years. It has been found expedient to clamp the aorta for very short periods of time. In 1950, Potts[18] employed his clamps to resect aneurysms of the thoracic aorta in five patients without a mortality. In 1951, Lam and Aram[19] clamped the thoracic aorta for twenty-four minutes while they resected a thoracic aneurysm. It is apparent from a review of the literature that either temporary or permanent aortic occlusion has been reserved for use in those patients in whom collateral circulation has been previously established. The use of temporary aortic occlusion as a means of controlling blood supply to facilitate surgical procedures, other than those concerned with the aorta itself, has not been adopted.

ANIMAL EXPERIMENTS

Procedures were planned to determine the useful safe time that the abdominal aorta might be occluded just above the celiac axis. In addition, the portal vein was occluded after the aorta and always released before the aorta. In all experiments this order and procedure were firmly adhered to in order to avoid the severe congestion which results when this order is reversed.

The dogs were prepared by intravenous Nembutal induction, and were maintained throughout the surgical procedures on a mixture of oxygen and ether. The aorta was exposed at the crus of the left diaphragm through an upper midline abdominal incision, and a Potts clamp was applied across it just above the celiac axis. One minute later the portal vein was similarly occluded by means of another Potts clamp. Lobes of the liver were then severed by means of a scalpel with practically no bleeding. The major hepatic veins and biliary

radicles were then sutured in order to occlude them so that hemorrhage and bile leakage would not follow the removal of the clamps. Gelfoam was applied and the clamps were removed.

A total of eighteen dogs were used in this study. By means of aortic and portal clamping, subtotal hepatectomy was safely and rapidly accomplished without blood loss. A maximum safe time of aortic occlusion was found to be twenty minutes; when the occlusion was extended to thirty minutes, fatalities occurred. When forty minutes of occlusion was employed, the mortality was 100 per cent.

In order to increase the safe time of occlusion beyond twenty minutes, the aorta and portal vein were occluded for ten-minute intervals to allow time for recovery before the next clamping. Judging from the appearance of the vessels along the stomach, it was apparent that at least twenty minutes was required for the circulation to return to normal. By this method the time of total occlusion could be extended to forty minutes without a fatality. When less than twenty minutes was allowed for recovery between clampings, fatalities occurred. It would appear that when the recovery period is too short there is a cumulative effect, as indicated by a failure of circulation to return rapidly in the omentum, stomach, and bowel. This would prolong the effect of previous occlusions if the recovery period is inadequate.

MICROSCOPIC FINDINGS

Microscopic findings may be briefly summarized as being confined primarily to the liver and kidneys. In each animal subjected to aortic and portal-vein occlusion, some change was noted; the degree of microscopic findings was the most profound in the animals which expired as a result of the aortic clamping.

In all animals surviving aortic occlusion the histologic findings were limited to the kidney. These findings consisted of casts in the collecting tubules and evidence of minimal degeneration of the tubular epithelium. In all animals dying as a direct result of aortic occlusion, histologic changes were found in the liver and kidney. This would lead us to believe that the liver plays a major role in the fatalities encountered. In these animals, areas of focal necrosis were found in the liver.

The course of the animal experiments and the ease of hepatic resection with the method described were encouraging. Accordingly, aortic and portal-vein occlusion was employed in two human patients.

CASE REPORTS

CASE 1.—A 70-year-old Negro man was hospitalized with a history of a gastrectomy for carcinoma three years prior to admission. Preoperative x-ray examination indicated that he had a recurrent carcinoma involving the left lobe of the liver without other evidence of metastasis. Exploratory laparotomy was performed on Sept. 27, 1952. Evidence of metastatic carcinoma was found to be present, and resection of the left lobe of the liver was undertaken. In this patient, total gastrectomy had been performed prior to this operation; hence, the approach to the abdominal aorta was accomplished without difficulty by incision of the peritoneum overlying the crus of the left diaphragm. By blunt dissection, two inches of the abdominal aorta was exposed. The celiac axis was identified, and a Potts clamp was

applied just above it. (The clamp was pushed against the vertebral column before the jaws were closed to prevent slippage and incomplete clamping.) Following closure of the clamp, no pulsations could be felt in the aorta below the site of application. In a patient in whom the anatomy is essentially normal, the approach to the abdominal aorta above the celiac axis is more difficult. Such a situation is described in the second case report. The portal vein was exposed by a retro-duodenal exposure. This was accomplished by incising the peritoneum lateral to the second portion of the duodenum and reflecting the duodenum toward the midline. A Potts clamp was then applied to the portal vein.

The entire left lobe of the liver was then removed by clamping across the liver with curved Kelly hemostats and excising distal to the clamps. Simple ligation of the structures within the clamps, namely, the major arteries, veins, and biliary ducts, was performed, and the clamps were removed. Gelfoam was applied to the cut surface of the liver. The portal-vein and aortic clamps were removed, and no bleeding occurred. The total time of aortic occlusion was ten minutes. The patient's postoperative course was uneventful, and he was discharged on the seventh day. A complete battery of liver function tests remained unchanged, as were also the urinary output, specific gravity, blood urea nitrogen, and phenolsulfonphthalein test. The only finding worthy of comment during the operative procedure was an increase in the patient's blood pressure of 40 mm. Hg while the clamps were in place. This returned to normal upon release of the clamps. Continuous electrocardiogram tracings (Lead II) remained normal throughout the entire procedure.

CASE 2.—A 67-year-old white man entered the hospital on Oct. 24, 1952, with a history of forty-three pounds weight loss, vomiting, and epigastric pain for four months. A diagnosis of carcinoma of the fundus of the stomach with almost complete obstruction of the cardia was established during the preoperative work-up. The patient received multiple transfusions of whole blood, serum albumin, and parenteral feedings. At operation the diagnosis was confirmed and, in addition, two metastases to the left lobe of the liver were seen. The esophagus was involved as well as the suprapancreatic lymph nodes. Accordingly, the abdominal incision was extended into the chest to provide additional exposure. The omentum, spleen, 80 per cent of the pancreas, and the entire stomach with the lower one-fourth of the esophagus were resected en bloc. An end-to-side esophagojejunostomy was performed to re-establish continuity of the gastrointestinal tract. A jejunojejunostomy was also performed to by-pass the previous anastomosis. The use of a thoracoabdominal incision facilitated the approach to the upper abdominal aorta.

The aorta was clamped just above the diaphragm. The portal vein was exposed, as in the previous case, and also occluded by means of a Potts clamp. The left lobe of the liver was removed, as in the first case, with such minimal blood loss that it was barely sufficient to stain a sponge.

In other patients the abdominal aorta was exposed in this region for the purpose of establishing a standard technique. The gastrohepatic ligament is identified and the left gastric artery located. The ligament is incised just above the artery, and through this opening the aorta can be palpated. The peritoneum overlying the aorta is incised and dissected from the aorta up to the level of the diaphragm. The clamp may now be applied. It is important that the clamp be pushed against the vertebral column in order that the entire aorta be occluded and also that slippage be avoided. Furthermore, if large tumors or other technicalities make the abdominal approach difficult, the combined thoracoabdominal approach may be accomplished by incising the diaphragm or by making the standard thoracoabdominal incision.

In this second case the aorta was occluded for ten minutes. Blood pressure response during the aortic occlusion was increased 60 mm. Hg and returned to normal upon release of the aorta. Postoperatively, the urine output was diminished to 300 c.c. during the first twenty-four hours. This increased uneventfully during the next three days with return to a normal urinary output. On the third day the thoracotomy tube was removed. The patient was eating small amounts of food by the fourth day, and he passed a small but normal

stool. On the fifth day the patient developed signs and symptoms of a mesenteric thrombosis. The abdomen was explored, and a twelve inch loop of necrotic jejunum was found. This was resected, and no other abnormalities were noted within the abdomen. The postoperative course was uneventful until three days later when the patient's condition rapidly deteriorated. He expired without evidence of abdominal pain.

At autopsy the entire small bowel was found to be gangrenous. Whether or not this was the result of the aortic clamping we cannot say, but the possibility must be accepted in the absence of evidence to the contrary. The superior mesenteric artery in cross section showed an arteriosclerotic plaque which occupied about four-fifths of the lumen. A soft unattached clot was found in the narrow lumen which apparently completed the vascular obstruction. It should be noted that heparin was not used after the first resection, and we feel that this was an error which allowed the final and fatal mesenteric occlusion. In the future, Depo-Heparin will be employed routinely following aortic clamping in the elderly patient to avoid this complication.

SUMMARY

A method of obtaining abdominal hemostasis to allow surgery in a bloodless field has been outlined. Application of this principle has one limiting factor, namely, that of time. The use of aortic occlusion has made subtotal hepatic resection technically easy. Furthermore, if the surgeon is prepared to occlude the aorta and portal vein, relatively hazardous dissections may be performed with confidence that no hemorrhage in the abdomen is uncontrollable. This is the most valuable use of the method at the present time. It is apparent that, regardless of the risk of employing aortic occlusion, it cannot add to the mortality of uncontrolled hemorrhage. This method can be applied below the diaphragm if each surgeon will familiarize himself with the approaches to the abdominal aorta as outlined.

In this preliminary report it is too early yet for us to be able to evaluate the added risks that this method may superimpose on abdominal surgical procedures. No thrombotic complications were encountered in any of our experimental animals, but it is suggested that heparin be used routinely postoperatively when aortic occlusion is used in elderly patients. Our further experiences will be reported at a later date.

CONCLUSIONS

1. Eighteen dogs were subjected to temporary aortic and portal-vein occlusion. Subtotal hepatectomy was easily accomplished without blood loss.

2. In the experimental animal the aorta above the celiac axis and the portal vein have been occluded for twenty minutes without a fatality.

3. Using intermittent occlusion, the time can be extended to forty minutes in dogs without lethal effects. When employing ten-minute occlusions, the clamps must be released a minimum of twenty minutes between clampings to prevent cumulative effects.

4. Microscopic findings in the liver and kidneys occurred after lethal aortic occlusion, and death was thought to be due at least partially to liver failure.

5. Two cases are reported of human beings in whom the left lobe of the liver was resected after the aorta had been occluded above the celiac axis.

6. Postoperative heparinization is suggested for elderly patients following temporary aortic occlusion.

7. Aortic occlusion is offered as a possible solution when uncontrollable hemorrhage is encountered during hazardous abdominal procedures or when it occurs secondary to trauma.

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EXPERIMENTAL AUGMENTATION OF CORONARY FLOW BY RETARDATION OF THE ARTERIAL PRESSURE PULSE*

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NUMEROUS surgical methods for increasing the blood supply to the myocardium of persons suffering from coronary insufficiency have been reported. Among these are the attempts to increase the extracoronary collateral supply to the muscle by the induction of pericardial adhesions[1] or the suturing of such vascular structures as the omentum,[2] muscle flaps,[3] or lung[1] to the surface of the heart. The efforts to stimulate the growth of collateral anastomoses to the coronary system by implanting one of the internal mammary arteries into the ventricular myocardium[4, 5] have yielded equivocal results. A new approach, used by Beck and associates,[6] perfuses the coronary capillary bed in a retrograde fashion by arterialization of the coronary sinus. This procedure is not yet fully developed, nor has it been finally evaluated. For this reason, an investigation was undertaken to determine whether the blood supply through narrowed coronary arteries could be improved by delaying the arterial pressure wave so that it arrives in the coronary arteries during diastole. This was accomplished by perfusing the coronary artery from one of the systemic arteries by interposing a suitable length of rubber tubing to delay the transmission of the pulse wave.

HEMODYNAMIC ANALYSIS

It has long been known that contraction of the left ventricle not only furnishes the pressure head for driving blood into the coronary arteries, but also offers resistance to coronary flow during systole. Since the pressure source for and the resistance to coronary flow have a common origin, the measurement of phasic flow is the only method that can permit evaluation of the determinants of coronary flow during successive phases of the cardiac cycle.[7]

The upper solid line curve (P_1) of Fig. 1 is the aortic pressure curve which represents the central coronary perfusion pressure. The lower solid line curve (Q_1) is the phasic flow pattern as obtained with an orifice meter.[7] It will be noted that during systole the coronary blood flow is less than during diastole, in spite of the fact that the pressure head is greater. This demonstrates that the peripheral coronary resistance is greatest during myocardial contraction. With subsequent ventricular relaxation and diminution of peripheral resistance, coronary flow rises sharply and reaches its maximum,

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even though the pressure perfusing the coronary arterial tree at this time is lower than at the previous systolic peak. It is during this diastolic period, and until the onset of the next systolic contraction, that the myocardium receives the major portion of its blood flow.

It would seem reasonable, then, to assume that if one were able to perfuse the coronary bed with higher pressures during diastole when resistance is lower, a greater flow could be obtained during this portion of the cardiac cycle. In addition, one would expect that a higher pressure applied during this period of time would dilate the coronary vessels to a greater degree. The dilated coronary bed would then be expected to carry more blood, and this would again increase the flow. It, therefore, would be desirable to perfuse the coronary bed with pulse pressures which are not only out of phase, but which also have a high peak.

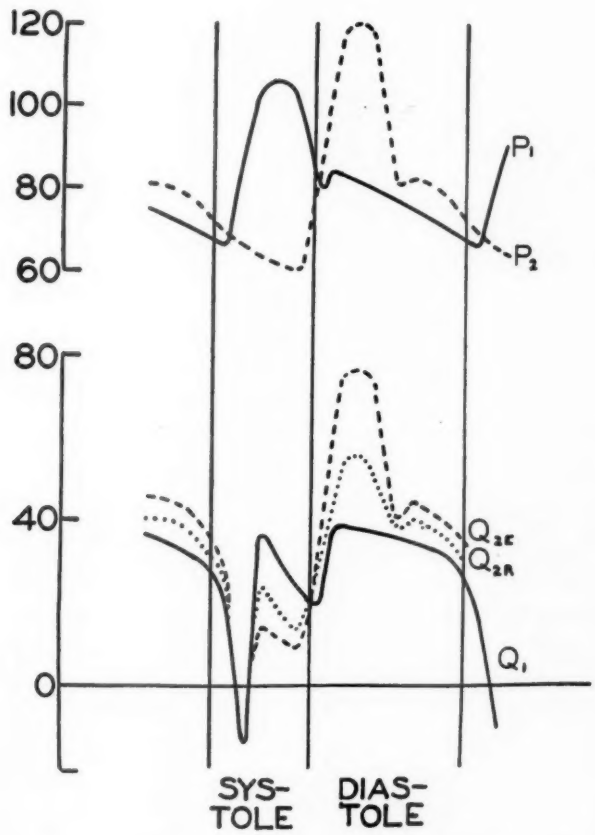

Fig. 1.—Heavy lines indicate normal aortic pressure (P_1) and phasic coronary flow (Q_1) after Gregg.[7] Dashed and dotted lines indicate predicted flows when the anterior descending coronary artery is perfused with pulse pressure out of phase with myocardial systole. P_2 represents proposed delayed coronary pressure; Q_{2R}, calculated flow in presumed rigid coronary system; Q_{2E}, calculated flow in presumed elastic coronary system.

The magnitude of the expected increase in coronary blood flow can be predicted on physical principles if we assume a delayed and peaked femoral pressure curve such as might be achieved experimentally. In Fig. 1, this curve (broken line, P_2) is superimposed over the normal curve. The systolic peak

is somewhat higher than that of the original aortic curve, but the mean pressure throughout the cardiac cycle is the same.

By applying Poiseuille's law, which defines the moment-to-moment relationships of pressure and flow, a first approximation to the expected increase in flow can be calculated. Poiseuille's law[8] is:

$$P = \frac{8Lv}{\pi r^4} \times Q, \tag{1}$$

where P equals the pressure head, Q the flow of blood, L the length of the vessel being perfused, y the viscosity of the blood, and r the radius of the vessel, all expressed in centimeter gram-second system units.

Let P_1 and Q_1, respectively, equal the pressure and flow at any instant in Fig. 1, and P_2 and Q_2 equal the projected pressure and the new flow, respectively. We can then solve for Q_2 from the following ratio of Poiseuille's law:

$$\frac{P_1}{P_2} = \frac{\frac{8Lv}{\pi r_1^4} \times Q_1}{\frac{8Lv}{\pi r_2^4} \times Q_2} \tag{2}$$

If we presume that L, the effective length of the coronary arterial tree, and v, the viscosity of the blood, do not change during a cardiac cycle, then the expression $\frac{8Lv}{\pi}$ is a constant and can be canceled to yield the expression

$$Q_2 = Q_1 \left(\frac{P_2}{P_1}\right) \times \frac{r_2^4}{r_1^4} \tag{3}$$

That is to say, if we want to know the flow at any instant during the cardiac cycle when a new pressure is being applied, we must know the previous pressure, the previous flow, the new pressure at that instant, and the effective radius of the coronary bed under the new pressure, as well as what it was under the original pressure.

The first three variables of this equation are immediately available from Fig. 1. The effective radius of the coronary bed, however, is information which we do not have. We can, however, attempt to calculate the limits between which the new flow curve must fall. The lower limit would be the flow, in a system in which the elasticity is zero, such that there would be no change in radius when an increased pressure was applied. This would mean, then, that the ratio $\frac{r_2^4}{r_1^4} = 1$, and therefore $Q_{2r} = Q_1 \left(\frac{P_2}{P_1}\right)$ where Q_{2r} is the flow through an assumed rigid coronary bed (plotted in Fig. 1 as a dotted line). We can calculate the upper limit if we assume that the coronary bed is as elastic as the most elastic artery that we know in the body, that is, the arch of the aorta, since information about the elasticity of this structure is available. Numerous studies[9, 10] have shown that when a closed section of the arch of the aorta is filled with fluid and the pressure is raised from 0 to 100 mm. Hg, then the volume is roughly doubled. Green, Gregg, and Wiggers[11] have shown that the change in volume of the anterior descending branch of the left coro-

nary artery is directly proportional to the change in pressure over the range from 20 to 140 mm. of mercury. Combining these two observations, we can write as an upper limit to the distention due to pressure.

$$V_2 - V_1 = V_1 \left(\frac{P_2 - P_1}{100}\right) \tag{4}$$

where V_2 is the volume of the coronary bed at pressure P_2, and V_1 is the volume at a lower pressure, P_1. Dividing Equation (4) by V_1 and squaring both sides we obtain

$$\left(\frac{V_2}{V_1}\right)^2 = \left(1 + \frac{P_2 - P_1}{100}\right)^2 \tag{5}$$

Since the volume of a cylindrical vessel is

$$V = \pi r^2 L \tag{6}$$

and, if the length remains constant during a volume change, then the radius ratio can be found by dividing two equations of this form, thus:

$$\frac{V_2}{V_1} = \frac{r_2^2 L}{r_1^2 L} = \frac{r_2^2}{r_1^2} \tag{7}$$

Squaring both sides of Equation (7) we get

$$\frac{V_2^2}{V_1^2} = \frac{r_2^4}{r_1^4} \tag{8}$$

Substituting this value of the volume ratio in Equation (5)

$$\frac{r_2^4}{r_1^4} = \left(1 + \frac{P_2 - P_1}{100}\right)^2 \tag{9}$$

Then Equation (3) becomes

$$Q_2 = Q_1 \left(\frac{P_2}{P_1}\right) \times \left(1 + \frac{P_2 - P_1}{100}\right)^2 \tag{10}$$

We can now solve this equation for Q_2 for a series of points, and draw the upper limit of the flow curve Q_{2E} on Fig. 1, which would represent the flow through this arterial bed if this system were the most elastic possible. The expected flow curve then must fall somewhere between these two limits. Obviously, flow is somewhat diminished during the latter part of systole, but definitely increased during diastole. By measuring the areas under these flow curves, it was found that we could expect an increase in flow somewhere between 20 and 40 per cent.

EXPERIMENTAL METHODS

Since the increase in flow realized depends on the elasticity of those portions of the coronary bed which offer the largest flow resistance, and since this cannot be evaluated mathematically, a method was devised for determining the gain in flow experimentally on anesthetized dogs. The thorax was opened under proper artificial respiration. The experimental setup is diagrammatically illustrated in Fig. 2. A large metal cannula was inserted through the bracheocephalic artery into the arch of the aorta of the dog. This led through a Y-tube to the orifice meter and from the orifice meter to the left circumflex coronary artery which we cannulated at a point 2 or 3 mm. beyond where it arose from the left common coronary artery. It thus was possible to perfuse the left circumflex coronary artery with aortic pressures

similar to those normally prevailing. The blood circuit from the aorta to the cannula in the left circumflex coronary artery is a rigid system and the blood is an incompressible fluid; therefore, the time delay in the arrival of the pulse to the left circumflex coronary artery is negligible. Since the central coronary pressure normally supplying the coronary bed is the same as aortic pressure, this enabled us to study, as others[12, 13] have done, the normal flow through the left circumflex coronary artery.

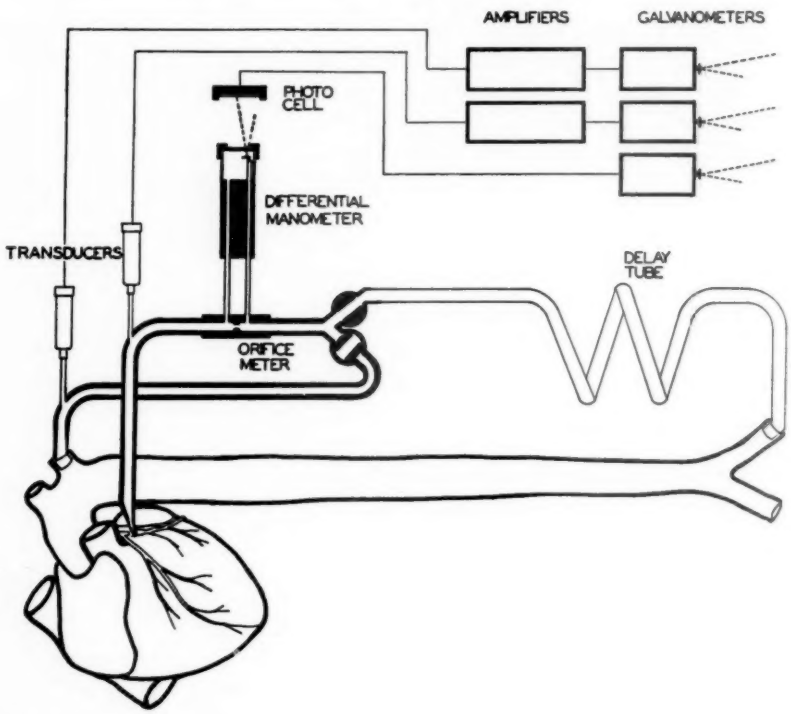

Fig. 2.—Schematic diagram of experimental setup. (Discussion in text.)

To accomplish the perfusion of the coronary artery with a delayed pressure pulse, one or both femoral arteries were cannulated. This blood was led through a rubber tube, acting as a delay tube, to the other limb of the Y and through the orifice meter to the same cannula in the left circumflex coronary artery. Since normally the transmission time of the pulse down the elastic aorta to the femoral arteries is from .05 to .07 second, and since a further delay of any desired length of time could be obtained by using appropriate lengths of rubber tubing to connect the femoral arteries with the Y-tube, it was possible to perfuse the coronary artery with pulsatile pressures out of phase with myocardial systole. In some experiments an adjustable orifice meter and differential manometer were used in order to measure phasic left circumflex coronary inflow.

In other experiments, aortic pressures were recorded from a transducer in the cannula from the aorta, and coronary pressures were recorded from a

transducer in the cannula to the coronary artery. A Hathaway Recording System[14] was used. In order to correct for the inherent nonlinearity of the orifice meter and differential manometer, a selenium photoelectric cell was introduced into the optical circuit of the flowmeter and the output of this photoelectric cell was led to one of the optical galvanometers of the Hathaway Recording System. By empirically adjusting the intensity and angle of the incident beam on the photoelectric cell, it was possible to correct the output of the flowmeter automatically so that the record would be a linear recording of the phasic flow through the system.

In four other experiments, precisely the same setup was used except that a rotameter was employed to measure mean flows through the left circumflex coronary artery.

In an attempt to design a satisfactory delay line, the use of various types of tubing was explored. It was found that latex rubber surgical tubing, 3 mm. inside and 5 mm. outside diameters, transmitted the pulse wave at a velocity of about 20 M. per second and permitted use of comparatively short lengths of the tubing from 80 to 120 centimeters. To maintain the peaked form of the pulse wave in the delay line, it was important that the junctions be constructed so as to minimize wave reflections.

RESULTS

Seven dogs were used to explore the mean flows by using a photoelectric bubble flowmeter[15] in a circuit similar to that shown in Fig. 2. A great deal of difficulty was encountered in obtaining pulse forms that resembled what we desired; because of the comparatively long lengths of external rigid tubing, the effective mass of the experimental circuit was too high. Nevertheless, in some of the experiments it was found that, when the left circumflex coronary artery was perfused with delayed pulses, some small increase in flow (up to 11 per cent) was occasionally observed.

In nine animals good pulse contours were obtained by reducing the effective mass of the external rigid circuit. This was done by reducing the length to about 30 cm. and increasing the diameter to about 1 centimeter. In each of fifty-six separate observations, blood flow through the left circumflex coronary artery was increased when this artery was perfused with a pulse pressure out of phase with the aortic pressure, as compared with the control perfusion when the pulse pressure was in phase with the aortic pressure. The increase in all of these observations varied between 22 and 53 per cent. Precautions were observed to rule out consequences such as changes in temperature of the blood perfusing the coronary artery and the dilating effect of temporary myocardial anoxia immediately preceding the observed coronary flow. Sections of a typical record of one of these experiments using the setup illustrated in Fig. 2 are shown in Fig. 3. In segment *A*, the coronary pressure is in phase with the aortic pressure, but it is slightly distorted due to its transmission through the meter. The flow rapidly drops to below zero in the early part of systole. After this, forward flow is re-established and there is some flow into the coronary artery during the

latter part of systole. At the onset of diastole, however, the flow rises rapidly and the major portion of the coronary blood flow occurs during this period. In segment *B*, Fig. 3, the coronary pressure is out of phase with the aortic pressure, the peak occurring during myocardial diastole. The phasic flow again rapidly drops to below zero in the early part of systole, but remains low throughout this entire period. At the onset of diastole the curve rises rapidly and reaches a peak which is almost double that seen in segment *A*. Obviously, the diastolic gain in flow exceeds the loss during systole. The phasic flow curves are distorted by the natural frequency of the differential manometer, which can be seen to be about 20 cycles per second. Unfortunately, the frequency response and the

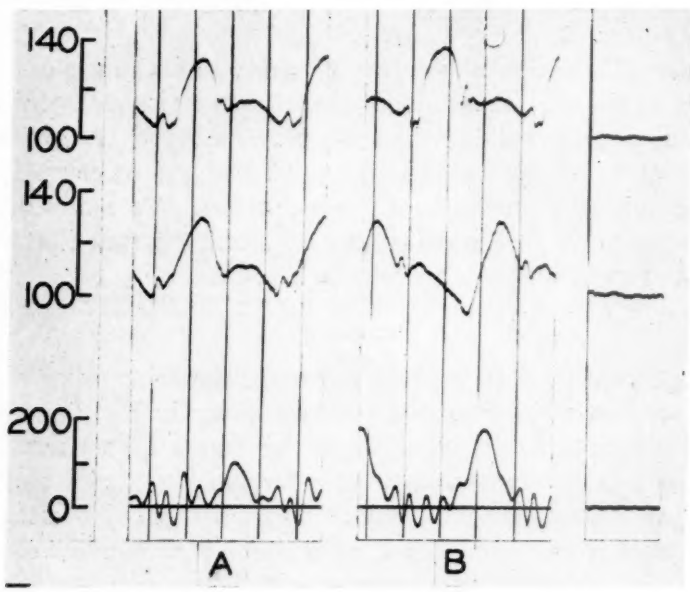

Fig. 3.—Segments of record from Dog 20. Upper curves represent aortic pressures in millimeters of mercury; middle curves, coronary perfusion pressures in millimeters of mercury; lower curves, phasic flow as recorded with an orifice meter in cubic centimeters per minute. Segment *A* shows coronary perfusion pressure in phase with aortic pressure; segment *B* shows coronary perfusion pressure out of phase with aortic pressure. Time lines represent 0.1 second. Mean flow is 53 per cent greater with delayed pulse.

damping of the differential manometer was inadequate to record faithfully the phasic flows. This inadequacy, however, would not affect the recorded mean flow and still would give a qualitative indication of the actual phasic flow. The mean coronary pressures in segments *A* and *B* of Fig. 3 are, respectively, 109 and 105 mm. of mercury. The mean flow in segment *A* is 36 c.c. per minute, and in segment *B* it is 55 c.c. per minute, an increase of 53 per cent over the control.

Sections of a record from an experiment in which a commercially available rotameter was used to measure blood flows are shown in Fig. 4. As can be seen from the record, the rotameter records, not absolute mean flows, but rather a sine curve from which the mean flow can be read by drawing a line through the middle of the curve. In segment *A*, the coronary pressures are in phase with the aortic pressures and are only slightly distorted by passage

through the flowmeter. In segment *B*, the coronary pressures are out of phase with the aortic pressures, their peaks falling just after closure of the aortic valves. Although the peak is somewhat higher than that seen in segment *B* of Fig. 3, it is not delayed as much. In segment *A* the mean coronary pressure is 112 mm. Hg and the mean flow is 35 c.c. per minute. In segment *B* the mean coronary pressure is 110 mm. Hg and the mean flow is 44 c.c. per minute, an increase of 26 per cent.

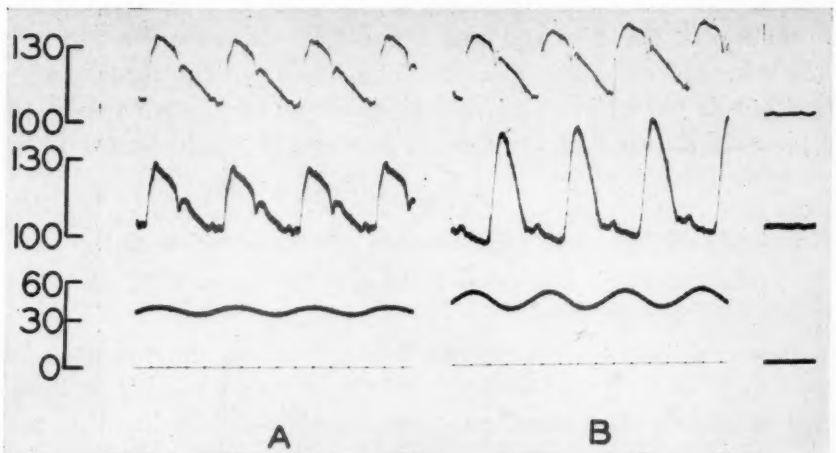

Fig. 4.—Section of record in Dog 23. Upper curves represent aortic pressures in millimeters of mercury; middle curves, coronary perfusion pressures in millimeters of mercury; lower curves, mean flow as recorded with a rotameter in cubic centimeters per minute.
Section *A* shows coronary perfusion pressure in phase with aortic pressure; section *B* shows coronary perfusion pressure out of phase with aortic pressure. Mean flow is 26 per cent greater with delayed pulse. Note that rotameter does not follow phasic flow changes.

DISCUSSION

The results of our experiments show that if it were possible to perfuse the coronary bed with peak systolic pressures during myocardial diastole an increase of flow through the coronary bed could be expected. This demonstration warrants the consideration of the possible development of a surgical procedure for improving coronary flow in persons suffering from coronary insufficiency. The pathologic changes of coronary sclerosis are such that it is entirely within the realm of possibility that this would have application in the surgical treatment of human arteriosclerotic heart disease. The atheromatous plaques in the coronary vessels are almost invariably restricted to the main-stems of the coronary arteries or to their immediate large branches. Over 50 per cent of the occlusions may be found within 3 cm., and 80 per cent within 6 cm., of the coronary ostia.[16, 17] About 66 per cent of all occlusions occur in the left anterior descendens.[17, 18] The distal portion of the coronary arterial tree, that portion imbedded in the myocardium, exhibits only minimal disease process. Further, the sclerotic process rarely occurs in a diffuse fashion throughout the epicardial arteries, but rather as more or less discrete plaques with areas in between available for anastomosis. The results of the pathologic process in the proximal portion of the coronary bed are a decrease in the mean perfusion pressure available to the coronary bed by the increased resistance of this seg-

ment and, thus a reduction of the coronary blood flow. Several arteries could be used to effect a direct anastomosis to the left coronary artery, such as the internal mammary, the splenic, the inferior epigastric, or one of several left intercostals. Any of these or a combination could be long enough to effect some delay in the arrival of the pulse wave to the coronary artery. Further, such an anastomosis, with the coronary arteries between the coronary ostia and the point where epicardial vessels descend into the myocardium, should effect a significant improvement in flow, because it would be possible to by-pass a portion of the diseased vessel and thus decrease the over-all resistance of the diseased coronary circuit. The improvement resulting from the direct anastomosis would have to be multiplied by the improvement resulting from the phase shift, so that the final improvement would be even greater.

SUMMARY

1. The phasic extravascular compression of the intramyocardial branches of the coronary artery causes increased resistance to flow during systole and decreased resistance during diastole.

2. It appeared that if it were possible to perfuse the coronary bed with systolic pressures during myocardial diastole, so as to be able to take advantage of the markedly decreased peripheral resistance during this period, an increase in coronary flow could be expected. This could be accomplished, for example, by delaying the arterial pressure peak long enough so that it would occur during diastole.

3. A theoretical analysis of the problem on the basis of Poiseuille's law led to the prediction that 20 to 40 per cent increase in flow through the left coronary artery might occur.

4. A delay of the pressure pulse so that the systolic peak was held back until diastole was achieved in twenty-six dogs by connecting the femoral artery by a proper length of tubing to the cannulated left circumflex artery.

5. Left coronary artery flows were studied with an orifice meter in order to record phasic flows and with a rotameter to record mean flows. It was found that the experimental data confirmed the theoretical analysis and that augmentation of flow was quantitatively and qualitatively as predicted by this theory.

6. It is suggested that this principle may prove surgically feasible as a means of improving coronary blood flow in arteriosclerotic heart disease.

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CLOSED LOWER LEG AMPUTATIONS IN ARTERIAL INSUFFICIENCY

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A LOWER leg amputation at the site of election, about 15 cm. distal to the tibial tubercle performed by primary closure, has not been generally accepted in our clinic as a good amputation for the average patient with obliterative arterial disease, secondary to arteriosclerosis or thromboangiitis obliterans. Instead, most lower extremity amputations have been the low thigh supracondylar type, because at this level primary healing is obtained in the great majority of cases. Failure to achieve this primary healing in many of the lower leg amputations in the past and the breaking down of the skin over the end of the tibia due to friction from the prosthesis, especially in patients with poor arterial circulation, have been the chief reasons for not performing the lower leg type of operation. With the realization, however, of the greater functional advantage of this type of amputation because the knee joint is preserved and of the considerable enhancement of primary healing because of the advent of antibiotics, we recently have attempted to re-evaluate it in a selected group of patients.

An important landmark of progress toward more conservative amputations in peripheral arterial deficiency was the development of proper indications and technique for performing transmetatarsal amputations by McKittrick and associates,[1] and by Warren and his group.[2] In 1950 Silbert and Haimovici[3] reported sixty-seven closed mid-calf amputations in which primary healing was obtained in 70.1 per cent of the cases and delayed healing in 26.9 per cent. No patient required reamputation at a higher level, and a high incidence of rehabilitation was obtained.

Procedure.—To investigate the results in the relatively small number of closed lower leg amputations which have been performed at the Massachusetts General Hospital in recent years, those cases in which operations were carried out in the five-year period from 1947 through 1951 have been reviewed and followed up. This series totals sixteen cases as compared with a total of approximately 205 cases of supracondylar thigh amputation during this same period. During these years there has been no special attempt to carry out a large number of closed lower leg amputations for vascular disease, since it was felt by a majority of the members of the peripheral vascular group that the results would be poor and the mortality and morbidity high.

The techniques have varied slightly. In general, the tibia has been divided approximately 15 cm. below the tibial tubercle, while the fibula was

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sectioned 1.5 to 2 cm. higher. In a majority of cases, the soft tissues were divided so that a long posterior and a short anterior flap were used. In one case a circular incision was made, and in two others a long posterior with no anterior flap was used. The latter incision places the linear scar directly over the anterior surface of the tibia, where it is subject to friction from the prosthesis; however, though both of these patients have done well, with no breakdown to date, it would seem unwise to place all incisions in this location.

This closed type of lower leg amputation should not be confused with the open or guillotine lower leg amputation, used for many years as an emergency procedure to halt spreading and uncontrollable infection.

Results.—Of this series of sixteen closed lower leg amputations, there were thirteen patients (81.2 per cent) in whom healing was satisfactory, although occasionally delayed, and in whom no further surgery was necessary. All stumps in this group were healed at the time of discharge from the hospital. Twelve of these patients (75 per cent) were able to wear prostheses satisfactorily, and there have been no breakdowns in the stumps in this group. These are classed as excellent and are summarized in Table I. The one individual who healed satisfactorily but did not wear a prosthesis was a 79-year-old woman, bedridden with cardiac disease, who had had a previous contralateral thigh amputation. It was hoped that the preservation of one knee would aid her in turning herself in bed. However, it is questionable whether this knee was of much value to her.

There were three failures (18.8 per cent), all requiring reamputation at a higher level. These cases will be discussed briefly, in an effort to elucidate the causes of failure.

CASE 1 (Unit 659329).—C. J., a 63-year-old man, had noted mild claudication in both calves for seven years, growing more severe six months before entry. He entered with a gangrenous ulcer of the inner side of the left heel, and another on the left fifth toe. He had unbearable rest pain unless the foot was dependent. The iliac artery pulsations were weak on both sides, and there were no pulsations palpable in the femoral arteries or below. This was confirmed by absence of oscillations in the thighs or legs. A left lower leg amputation was performed three weeks after entry, using a circular incision at 14 cm. below the knee. There was a little skin, muscle, or arterial bleeding at the time of operation. Necrosis of the anterior flap began on the eighth postoperative day, and a low thigh amputation was subsequently carried out. This incision also failed to heal, and an area of slough along the incision had to be débrided and the stump revised and shortened.

Comment.—This was a poor case for a lower leg amputation since the weak iliac and absent femoral pulsations indicated severe vascular insufficiency.

CASE 2 (Unit 717777).—L. F., a 60-year-old man, had had severe claudication in the left leg for eight months, with rubor and severe rest pain for two months. An ulcer appeared on the left heel four days before entry, and was found to be undermined by pus. Both femoral pulses were weak, and no femoral or pedal pulses were felt on either side. The necrotic ulcer was débrided, after which the infection cleared. Three weeks after entry a closed lower leg amputation was performed, using a long posterior and a short anterior flap, dividing the tibia 12 cm. below the tubercle. There was little bleeding at the time of amputation, and the operator was pessimistic as to its prognosis. The anterior flap became necrotic in six days and a thigh amputation was eventually performed.

Comment.—Here again the combination of weak femoral pulses and lack of bleeding at the time of operation indicated arterial obliteration of severe degree.

TABLE I. SUMMARY OF THE TWELVE SUCCESSFUL CASES IN THIS SERIES

PATIENT	AGE (YR.)	DIABETES	LOCATION OF AREA OF INFECTION ON OPERATED LEG	LOWEST PALPABLE PULSE	PREVIOUS OPERATIONS	RESULT OF LOWER LEG AMPUTATION
M. E.	52	Yes	Ulcer, great toe, plantar arch	Popliteal	Transmetatarsal	Primary healing, wearing prosthesis, 1 yr.
G. T.*	41	No	Ulcer, medial malleolus	Femoral	Lumbar sympathectomy	Primary healing, wearing prosthesis, 2 yr.
M. K.	67	Yes	Gangrene, dorsum, right foot; gangrene left great toe	Popliteal Popliteal	None Left great toe amputation	Bilateral lower leg amputation, using bilateral prostheses, well at 2½ yr.
C. C.	70	Yes	Gangrene, all toes and dorsum of foot	Popliteal	Guillotine of foot	Delayed healing, 1 mo., using prosthesis, 9 mo.
J. L.*	48	No	Gangrene, second toe	Femoral	Nerve-crushing for pain	Primary healing, using prosthesis, 5 yr.
Z. W.	58	No	Ulcer, dorsum of foot	Femoral	Lumbar sympathectomy	Primary healing, back to work on prosthesis, 2½ yr.
H. C.	57	Yes	Gangrene, fifth toe; sepsis, distal half of foot	Popliteal	Incision and drainage	Primary healing, back to work using a welding torch, used prosthesis until death from coronary, 1 yr.
M. G.*	24	No	Gangrene, toes and dorsum of foot	Femoral	None	Delayed healing, 1 mo., wearing prosthesis, 2 yr.
A. F.	70	No	Deep ulcer, lateral aspect of foot	Femoral	Ulcer débrided	Primary healing, used prosthesis 1½ yr. before death
M. G.	64	Yes	Gangrene, fifth toe; ulcer plantar surface of metatarsal heads	Popliteal	Guillotine of foot	Delayed healing, 3 mo., used prosthesis, 4 mo., then had contralateral low-thigh amputation, confined to wheel chair since
P. P.	56	No	Gangrene, toes; ulcer over medial malleolus	Popliteal	Guillotine at ankle, contralateral low-thigh amputation previously	Primary healing, using bilateral prostheses, at 3 yr.
H. W.*	61	No	Breakdown of transmetatarsal stump	Femoral	Transmetatarsal amputation (contralateral Gritti-Stokes amputation seven years before)	Delayed healing, prostheses, bilateral, 3 yr.

*Indicates private patients of R. R. L.

CASE 3 (Unit 680064).—E. A., a 67-year-old man, entered with mummification of all toes of the right foot. He had a mild diabetic condition and no pulses were felt below the femoral arteries, which were normal. Four weeks after admission a right transmetatarsal amputation was performed. Healing was delayed by necrosis of the dorsal flap. He was sent home on a conservative regime, but the area of necrosis advanced. He returned to the hospital two months after the initial amputation and a femoral arteriogram revealed patent vessels in the right leg down to the level of the ankle. Therefore, a closed lower leg amputation was performed, using a long posterior and a short anterior flap. This incision healed primarily and he was discharged on crutches without a prosthesis. Shortly after his arrival at home, he fell on the stump, and the incision slowly broke down over the next few weeks. He did not keep his follow-up clinic appointments and, when first seen two months later, the tibia was protruding through the incision. Two weeks after readmission the stump was revised and the tibia shortened. There was brisk bleeding from the skin edges at this time. Unfortunately, this incision became infected and had to be opened along its medial two inches. Because of persistent drainage and necrosis of skin edges a right low thigh amputation was performed.

Comment.—It is felt that success might have been achieved in this case but for the unfortunate fall on the lower leg stump shortly after the patient's discharge on crutches. This could probably have been avoided had he been sent home with a temporary prosthesis, as are a majority of amputees in this hospital.

DISCUSSION

On the basis of this small series of cases, it would seem that the lower leg amputation is a better operation than had been anticipated. It is probable that many of the patients who have been subjected to low thigh amputations in the past will be found to have proper indications for a closed lower leg amputation in the future. The recent experience of Silbert and Haimovici[3] would certainly indicate that this is true.

In considering the indications for a below-the-knee amputation and the causes of success or failure in our series, the following factors may be important.

Cause of Arterial Deficiency.—Of the thirteen patients with satisfactory healing of the stump, six had diabetes, five had arteriosclerosis, and one had thromboangiitis obliterans (G. T.). One patient (M. G.), a young woman of 24 years, had arterial thrombosis of unknown origin with excellent pulsating arteries at the site of amputation. Of the three unsuccessful cases, two patients had arteriosclerosis and one had diabetes. Thus, the cause of obliteration cannot usually be used as a prognostic factor.

Age of Patients.—Age at the time of amputation in the entire group varied from 24 to 70 years. The two 70-year-old patients were successfully rehabilitated, while the three failures were in patients in their sixties. Therefore, age gives no indication of the outcome, and old age in itself does not necessarily prevent satisfactory use of a lower leg prosthesis.

State of the Circulation.—The degree of arterial deficiency and the amount of established collateral circulation are the primary determinants of the success or failure of this procedure. Our experience indicates that the absence of a palpable popliteal pulse is not a contraindication to a mid-calf amputation, since the popliteal pulse could not be felt in six of the twelve rehabilitated patients (see Table I). On the other hand, a weak or absent

femoral pulse considerably reduces the chance of success, as noted in two of the three failures. In all of the successful cases the patients had good femoral pulses.

Severe intermittent claudication in the calf muscles and ischemic rest pain are not good indicators of prognosis, since they have occurred in both groups. Four of the twelve patients in whom the operation was successful and two of the three in whom it failed had severe rest pain before operation.

Rubor on dependency may help determine the severity of ischemia in conjunction with the other clinical findings, but alone it is not a reliable prognostic sign.

Adequate skin and muscle bleeding at the time of operation seems to be the best indicator of probable success, since it is the only direct measure of good collateral circulation at the site of amputation.

This series is not large enough to determine whether the lower leg stump is less painful than amputation at the low thigh, but the midcalf stump has proved to be very effective in making ambulation much easier with a prosthesis. Careful follow-up of the twelve successful cases indicates that all of these individuals have worn their prostheses satisfactorily to the time of writing or until they have died or become bedridden by intercurrent disease. This excellent degree of rehabilitation is a great deal better than our general experience with thigh amputations, when approximately one-half the men and a much smaller number of women ever learn to use a prosthesis.

SUMMARY

Sixteen closed lower leg amputations performed in the five-year period from 1947 through 1951 have been reviewed.

There were thirteen cases (81.2 per cent) of successful healing of the lower leg stump, and three failures (18.8 per cent) necessitating higher amputation. Twelve patients (75 per cent) satisfactorily learned to use a prosthesis.

Indications and contraindications are discussed. It is felt that intermittent claudication or absence of a palpable popliteal pulse are not contraindications, but that a weak femoral pulse or evidence of poor skin and muscle bleeding at operation indicate a poor prognosis.

Finally, it should be stated that, in our opinion, the low thigh supracondylar amputation is the operation of choice in the majority of patients with gangrene of the foot secondary to chronic obliterative arterial disease of the lower extremity. In cases where the collateral circulation of the foot is good, a below-the-knee amputation is recommended because of the better function that is obtainable with a prosthesis.

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A CRITICAL ANALYSIS OF END RESULTS IN FRACTURES OF THE FEMORAL SHAFT TREATED BY INTRAMEDULLARY NAILING

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DURING the past decade the operation of intramedullary nailing has been accepted as a procedure especially suitable for certain fractures of the middle three-fifths of the femoral shaft. When used under the proper circumstances, and in trained hands, the method is attended by a marked reduction in the time of recumbency and of hospitalization. Early weight-bearing is possible, and there is preservation of joint motion and muscle nutrition. Patients with multiple injuries are available for treatment which would be impracticable with recumbency. There is facilitation of patient transportation. Complications due to prolonged recumbency are avoided and there is a most beneficial stimulation to mental and physical well-being by the early return to normal activity.

There are arguments against the procedure which have prevented the universal use of the method even in selected cases and under optimum circumstances. The reduction and fixation are ordinarily accomplished by open operation which subjects the patient to the general hazards of such a procedure. In addition, there are technical difficulties peculiar to the nailing procedure, and these may cause operative and postoperative complications which can be disastrous.

There still remains a considerable difference of opinion as to whether the acknowledged risk of this operative procedure is justified even when conditions seem to indicate its use. It is our purpose to analyze critically the end results of fractures of the middle three-fifths of the femoral shaft treated by intramedullary nailing and to compare them with results obtained by conservative management with the use of traction suspension.

MATERIAL

During the past four years in an Army general hospital there have been 93 open intramedullary nailing operations performed in suitable femoral shaft fractures. Eighty-five of these patients have been followed for a sufficient period of time so that the end results are known. Of this group there were 65 procedures for recent fractures. Fifty-two of these were in closed fractures and 13 in open fractures after wound healing was complete. Twelve operations were performed because of old non-union of the middle three-fifths of the femoral shaft. Eight patients who are considered in a special category

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presented severely infected gunshot fractures with marked comminution and loss of bone. This latter group of patients was treated by thorough wound débridement and intramedullary nailing with all wounds left wide open for drainage. It has been our custom to use iliac bone grafts in the treatment of all of these fractures with the exception of the ones associated with open gunshot wounds.

Sex and Age.—There were 80 men and 5 women. The average age was 25.5 years, the oldest being 51 and the youngest 17 years of age. Sixty-nine patients were in the Military Service. Eleven were veterans and 5 were dependents of the Military.

Type and Location.—Thirty-two fractures were at the junction of the upper and middle thirds of the femur. Forty-six were located in the middle of the shaft and 7 were at the junction of the middle and lower thirds. In 48 patients the fractures were oblique or transverse. In 3 they were segmental with a small middle fragment. The fractures were designated as being of the comminuted type in 14 and of the butterfly fragment type in 20.

Time Interval and Type of Fixation.—The average time interval between injury and nailing in the entire group was fourteen weeks. The shortest was one week and the longest was in an old nonunion 242 weeks after injury. In the group of recent femoral fractures the average interval was 3.2 weeks. As fixation material we used the clover-leaf type of nail exclusively. A single nail was used in 53 patients, and in 12 cases two nails were nested together to achieve fixation in unusually large canals. In 14 patients there was supplementary wire fixation, and in 6 cases one or more screws were used for added stability.

END RESULTS

Wound Healing.—In 77 patients the wounds were closed postoperatively in the usual manner. In 2 cases there was slight drainage from the wound, but this promptly subsided and had no bearing on the results. Seventy-five wounds healed primarily. In the 8 patients with recent gunshot fractures the wounds were left open for drainage. A two-year follow-up investigation has revealed complete healing in 5 of these, but 3 present slight intermittent wound discharge.

Bone Healing.—The end results of the bone healing process in the various groups are recorded in Table I. In the entire series there was bone union in 80 patients (94.1 per cent). In the group of recent fractures there was only one case of non-union, giving satisfactory healing in 98.5 per cent. The time of apparent bone healing was recorded on the roentgenogram in 75 patients. The longest was fifty-two weeks and the shortest ten weeks, with an average of 17.4 weeks. In the group of patients with recent fractures the average time of union was 16.4 weeks.

Time of Nail Removal.—The nails have been removed in 39 patients. The earliest time of removal was five months and the latest eleven months, with an average of 7.8 months.

TABLE I. BONE HEALING

	ENTIRE GROUP (85)	RECENT FRACTURE (65)	OLD NON-UNION (12)	GUNSHOT FRACTURES (8)
Prompt union	76	62	8	6
Delayed union	4	2	1	1
Non-union	5	1*	3†	1‡

*Union after secondary operation.
†One patient.
‡Strong fibrous union.

Knee Motion.—One patient in this series had 3 operations for non-union. Another had a second nailing procedure before union was obtained. There were, consequently, in the entire group 82 knees which could be evaluated as to restoration of function. Of the entire group, 72 patients (87.8 per cent) had preservation of knee flexion beyond the right angle. In the group of recent fractures this amount of flexion was retained in 63 (98.4 per cent). Flexion of less than 45 degrees was recorded in only 2 cases (2.4 per cent).

Complications.—Refractures occurred in two patients, but these fractures eventually healed. There was absorption of bone at the fracture site with delayed healing in 3 patients, and this was attributed to an electrolytic reaction set up between the nails and the encircling wire loops used for supplementary fixation (Fig. 1). One patient developed an external rotation deformity of the lower fragment at the fracture site. One patient presented distraction of the fragments postoperatively, but this was subsequently corrected. One nail split while being inserted and was replaced at the original operation after roentgenographic check. Two patients sustained further femoral injuries postoperatively with bending of the nails when they fell from wheel chairs. These nails were straightened under anesthesia and the fractures went on to bone healing. No attempt at nail removal was made because of persistent slight deformity and, therefore, these femurs will present an additional problem in the eventuality of subsequent refracture. There were no pulmonary or renal complications. One patient had an exacerbation of an old femoral thrombophlebitis.

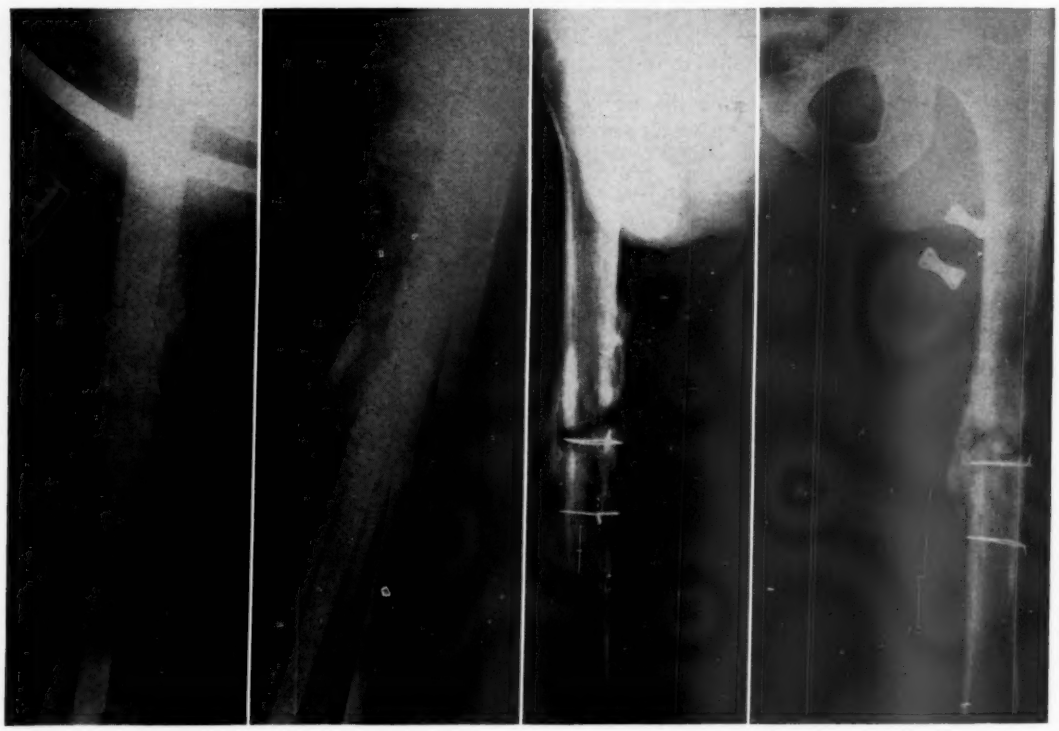
Time in Bed.—In the entire group the average time spent in bed postoperatively, was 3.6 weeks, the longest being twelve weeks and the shortest one week. In the recent fractures the average was 2.7 weeks; in the old non-union group, 7.7 weeks; and in the gunshot fractures, 4.3 weeks.

Time of Weight-Bearing.—Eliminating the patients who had non-union and those with associated amputations or major leg injuries, the average time of weight-bearing following operation in the entire group was 5.2 weeks, the earliest being one week and the latest sixteen weeks.

Time of Hospitalization.—Again eliminating the patients who went on to non-union or those with other major injuries which prolonged their hospitalization, the average postoperative hospital stay for the entire group was 22.7 weeks and, for the recent fracture group, 15.5 weeks.

Eventual Disposition.—There were 69 operations in 65 military patients. Fifty patients (76.9 per cent) were returned to military duty and 15 were dis-

charged from the Service. Of the 16 civilian patients, all returned to full activity. In military patients with recent fractures all were returned to duty except those with severe associated injuries which were the reason for discharge. The shortest time of return to duty was two weeks and the longest, due to secondary operation for non-union, was seventy weeks, with an average of 18.0 weeks.



A. *B.* *C.* *D.*

Fig. 1.—*A* and *B*, Postoperative anteroposterior and lateral films of middle third femoral fracture fixed by intramedullary nail and two supplementary wire loops. *C* and *D*, Seven months postoperative films showing delayed bone union with marked absorption of bone due to electrolytic changes between nail and wires. There was eventual solid union and never any clinical sign of bone infection. (Photographs by Letterman General Hospital photographic laboratory.)

Comparative Statistics.—In order to evaluate the functional results in this group of patients, comparison was made with results obtained by traction suspension in 21 similar fractures. Table II represents these comparative results. It will be noted that the patients treated by nailing spent approximately one-eighth the time in bed and one-third the time in the hospital compared with the conservatively treated group. The time of hospitalization in both groups is higher than it would be in civilian practice because the military patients must be kept in the hospital until they are ready for return to duty or discharge from the Service. The rate of primary bone union was considerably higher in the nailing group, the recovery of knee function was more satisfactory, and the percentage of patients returned to full activity was much greater than with conservative management.

TABLE II. COMPARISON WITH PATIENTS TREATED CONSERVATIVELY

	RECENT FRACTURES TREATED BY TRACTION SUSPENSION	RECENT FRACTURES TREATED BY NAILING	ENTIRE GROUP TREATED BY NAILING
Number of patients	21	65	85
Time in bed (weeks)	25.0	2.7	3.6
Time in hospital (weeks)	44.1	15.5	22.7
Primary bone union	17 (81.0 per cent)	64 (98.5 per cent)	80 (94.1 per cent)
Union after secondary operation	4	1	1
Non-union	0	0	4*
Mortality	0	0	0
Complications			
Renal	3		0
Pulmonary	0		0
Thrombophlebitis	0		1
Knee flexion			
90 degrees or more	7	63	72
45 to 90 degrees	9	1	8
Less than 45 degrees	5	0	2
Disposition	(20 patients)	(64 patients)	(81 patients)
Full activity	11	60	66
Limited activity	9	4	15

*One non-union nailed three times; one gunshot fracture with fibrous union.

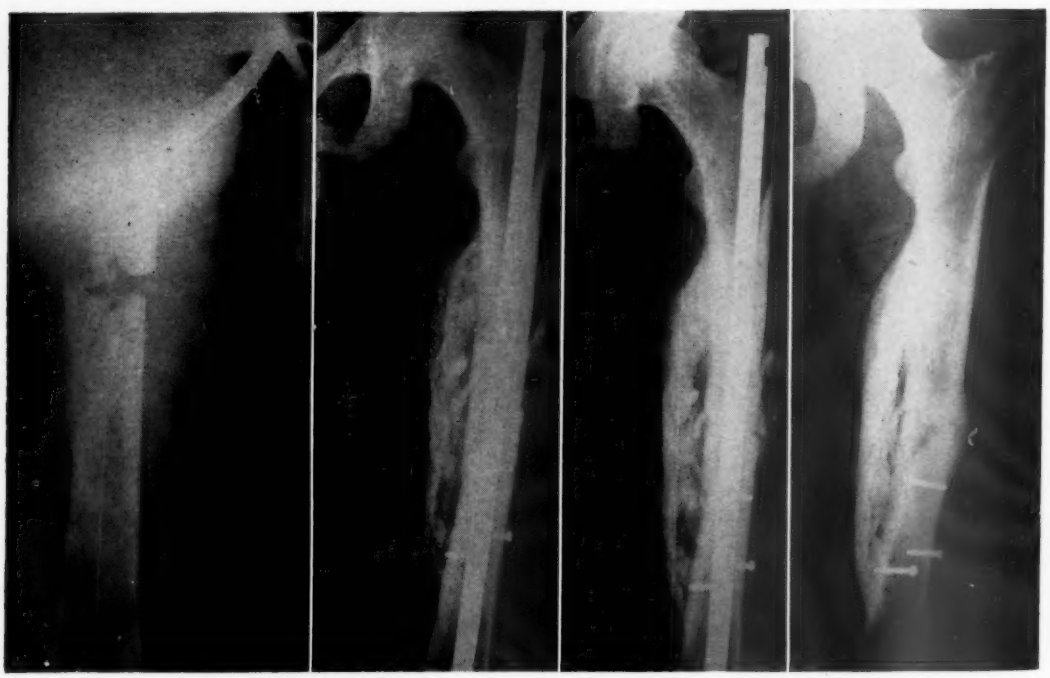
DISCUSSION

It must be emphasized that the procedure of intramedullary nailing in fractures of the femoral shaft must be reserved for properly selected cases in which the patients are to be treated by qualified surgeons under optimum operative circumstances. Only fractures in the middle three-fifths of the shaft are suitable. The general condition of the patient and the local operative site must be satisfactory for a major elective operation. The treatment is not indicated in open fractures before wound healing. In certain recent gunshot fractures which present exceptional features, such as extensive bone or soft tissue loss which prevent conservative management or prolonged suppuration due to inadequate fixation by traction suspension, the nailing procedure may occasionally be used provided all wounds are left open for drainage. It is not recommended as a routine procedure in these open cases even under optimum conditions. A more detailed account of this unique group of patients has been reported elsewhere.

Concerning the type of intramedullary fixation, it is our feeling that, whenever possible, a single nail of proper diameter for adequate fracture immobilization is to be preferred. In certain comminuted or butterfly types, supplementary wire or screw fixation may be necessary, but there is the danger of bone absorption due to electrolytic reaction at the fracture site with delay in bone union. Three of our patients were so affected. When the diameter of the canal is larger than the 12 mm. diameter of the largest available cloverleaf nail, we have employed two nested nails to produce stability. There have been no ill effects from this procedure, but it offers an even greater technical operative hazard. In 4 instances, where double nails of an imported stainless steel material were used, discoloration of the nails was apparent upon removal, but there was no other evidence of electrolytic reaction. This did

not occur when double nails of domestic material were employed. It is our feeling that whenever possible, any type of supplementary metallic fixation should be avoided.

Wound infection is always a possibility with such procedures. The fact that there was prompt healing of the two infections in this group with no untoward effect on bone union suggests that this complication is not a discouraging factor. The relatively good soft tissue covering of the femoral shaft apparently presents a better site of resistance to infection than more superficial structures such as the tibia and ulna. It is our feeling that this factor is one of the reasons for the suitability of femoral shaft fractures to the nailing procedure.



A. *B.* *C.* *D.*

Fig. 2.—*A*, Preoperative anteroposterior film of comminuted middle third femoral fracture. *B*, Two months postoperative film showing abundant callus on the inner surface of the fracture site and also well proximal and distal to the fracture. Fixation obtained by intramedullary nail and three metal screws. *C*, Six months postoperative film showing bone healing with marked medial bridging. *D*, At seven months the nail has been removed and bone union is excellent although there is some remnant of the fracture line. (Photographs by Letterman General Hospital photographic laboratory.)

The very large percentage of patients with prompt bone union following intramedullary nailing would seem to deny the claim that the procedure interferes in any significant way with the healing process. In at least three-fourths of our patients with recent fractures there was a tremendous accumulation of callus and new bone, chiefly on the inner surfaces of the fragments and often well above and below the fracture site (Fig. 2). This is probably the result of the mild local pressure at the fracture site due to muscle tension, but it appeared to be much greater than that which is seen in the healing process

by conservative treatment. Our use of iliac bone grafts in most of our patients may certainly be a factor and is, we believe, an argument for the employment of such grafts, but we have also seen this excessive bone proliferation in patients nailed elsewhere without bone grafts. Early weight-bearing may be an additional stimulating factor, but we have noted this overgrowth of callus and bone in amputee patients who have been unable to bear weight early. The response may well be due, at least in part, to stimulation of the nailing procedure itself. Certainly we have no evidence that intramedullary nailing retards the process of bone healing. The sixteen-week average time of apparent bone union on the roentgenogram compares very favorably with the time noted in similar fractures treated by other methods.

It is our feeling that in this group the nails were removed too soon in 3 patients and that this was the cause of refracture in 2 and at least a factor in the non-union in 1 patient. It is now our policy to avoid removal of nails until a minimal period of one year from the time of insertion. Wound infection is not an indication for nail removal, but adequate drainage of such wounds is imperative until healing occurs. Nails should be retained until definite union or non-union is assured, and we feel that ordinarily the minimal period of certainty, in spite of the roentgenographic appearance, is a full year. Nail removal at the end of this period is advisable because of the possibility of nail migration and the hazard of subsequent fracture and deformity with the nail in place.

There can be little doubt of the advantages of early weight-bearing from the functional and economic aspects. The stimulation to general well-being and morale is obvious, and the preservation of joint motion and muscle function is most desirable. In civilian practice the time of hospitalization and the economic stress to the patient can be considerably curtailed by the use of the method, and the average time of hospital stay will be much less than in this military group. Comparison of the respective complications, time of weight-bearing, time of hospitalization, and the functional recovery, in the nailing group with those in the group treated by traction suspension is most impressive.

Our very satisfactory results with this group of patients have not made us unmindful of the precautions essential to the nailing procedure and the inherent dangers of the method. Patients must be carefully selected and the operations performed by experienced surgeons under optimum conditions. Gunshot fractures should be treated in this manner only under exceptional circumstances and these wounds must be left open. When properly applied and skillfully executed the intramedullary nailing procedure has proved to be an historic advance in the treatment of fractures of the femoral shaft. The tremendous functional and economic advantages over treatment by conservative measures are sound justification for the calculated operative risk.

SUMMARY

1. The end results of a group of 85 femoral shaft fractures treated by intramedullary nailing have been evaluated.

2. Comparison has been made with results obtained in a group of patients treated by traction suspension.

3. When properly applied in selected cases by trained surgeons under optimum operating conditions intramedullary nailing is the treatment of choice in fractures of the femoral shaft.

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AXILLARY GLAND DISSECTION WITH PRESERVATION OF PECTORAL MUSCLES FOR CARCINOMA OF THE UPPER EXTREMITY

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THE purpose of this report is to demonstrate that an adequate axillary gland dissection for carcinoma of the upper extremity can be performed with preservation of the pectoral muscles. This is important, particularly for the working man, since the pectoral muscles contribute in large measure to shoulder strength. The pectoralis major functions in flexion, adduction, and inward rotation of the humerus, while the pectoralis minor serves to amplify shoulder girdle motion by depressing the scapula. Although a full range of shoulder motion can often be maintained following removal of these muscles, strength is moderately, or even seriously, impaired.

Whereas lymphatic channels draining the breast tissue permeate the pectoral fascia and muscles, thereby necessitating removal of these structures en bloc in surgery for cancer of the breast, this situation does not pertain for carcinoma of the upper extremity. Lymphatic channels draining the upper extremity accompany the blood vessels directly to the axillary node groups proper.† Accordingly, the only indication for eradication of the pectoral muscles during axillary dissection for carcinoma of the upper extremity is the facilitation of clean dissection of the axillary contents. Admittedly, in an obese person, it may be difficult or impossible to perform a scrupulous dissection and yet to preserve the pectoral muscles with nerve and blood supply intact. Also, in the case of the aged person, or of those for whom shoulder strength is of little importance, the prolonged dissection required to spare these muscles may not be merited. In general, therefore, this procedure may be limited to those patients who are middle-aged or younger, who are of medium or thin habitude, and for whom normal shoulder strength is a valuable asset.

It has been maintained that the preservation of the pectoral muscles creates a closed space, which is difficult to drain properly, and which, thereby, invites complications of serum accumulation, infection, and later fibrosis, with resultant permanent restriction of shoulder motion. However, it may be contended that meticulous hemostasis, adequate drainage, and an efficient pressure dressing will largely obviate these troubles. Indeed, should infection supervene through inadvertence, it may be so readily eradicated by an appropriate antibiotic that postinfection fibrosis with limitation of motion may be averted.

The opinions expressed in this manuscript are solely those of the author, and are not intended to represent the views of the United States Air Force Medical Corps or of any other governmental service.

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†Lewis, W. H.: Gray's Anatomy, Philadelphia, 1942, Lea & Febiger, pp. 701-703.

The following case report is presented to illustrate the points raised in the preceding discussion.

CASE REPORT

B. S., a 39-year-old white man, was seen in the surgical outpatient clinic on Aug. 13, 1952, for removal of a pigmented nevus on the outer aspect of the anterior surface of the right upper arm, at the junction of the middle and lower thirds. The patient stated that the lesion had been present for two or three years but, within the previous two weeks, had become slightly blacker in appearance and had developed some superficial crusts. On picking off the crusts, he provoked a small amount of bleeding. The lesion was excised in transverse direction, including a generous margin of surrounding skin and subcutaneous tissue, employing a field-block type of local infiltration anesthesia, which avoided infiltration directly into the area of the lesion. Pathologic study revealed the lesion to be a junctional nevus with malignant transformation.* It appeared to have been excised in its entirety.

On Sept. 3, 1952, re-excision of the previous excision site was carried out. At this time, the entire transverse scar was excised together with the underlying subcutaneous tissue and deep fascia covering the biceps muscle. This excision was carried out in a longitudinal direction, and was closed primarily under moderate tension. Concomitantly, a nonulcerated, shiny, firm, nodular lesion of the right malar region, which had been present for about four years, was widely excised for biopsy, with a clinical diagnosis of basal-cell carcinoma. Pathologic study of the excised scar and underlying fascia revealed no evidence of residual melanoma. The lesion from the right malar region was reported to be basal-cell carcinoma, which appeared to have been completely removed.† Both excision sites healed uneventfully.

On Sept. 15, 1952, the patient was admitted to the hospital for work-up preliminary to prospective prophylactic right-axillary-gland dissection. He had remained entirely asymptomatic.

Past history revealed that the patient had contracted both gonorrhea and syphilis in the late 1930's, and was adequately treated for the former, but was not treated for the latter until 1948, when he was given a course of penicillin therapy. Serology had been consistently positive to date. In addition, in 1949 he suffered a spontaneous pneumothorax, which was treated conservatively with ultimate full expansion, and without residual or recurrent difficulty. Bronchoscopy and repeated chest roentgenograms were within normal limits.

Family history was significant only in that the patient's father had had multiple "skin cancers" removed.

In regard to occupational exposure, the patient, prior to entering the Service eleven years previously, worked as a farmer, and was also employed at various odd jobs, including operating a filling station. He gave a history of more than average exposure to actinic radiations.

Physical examination revealed a red-haired, fair-skinned, thin, middle-aged man. Temperature was 98.6° F.; blood pressure 108/68; pulse 76; respiration 20; height 5 feet, 9½ inches; weight 120 pounds. There was a soft, pliable, obliquely placed, incisional scar 3 cm. in length across the right malar region, without evidence of persistent or recurrent basal-cell carcinoma. Three other tiny keratotic (proved by subsequent biopsy) lesions were present on the face: one on the left side of the bridge of the nose, the second in the center of the left lower lid, and the third in the left temporal region. Examination of the eyes, ears, nose, and throat was negative. There were no palpable cervical or supraclavicular lymph nodes. Heart and lungs were within normal limits, and abdomen was negative, as was rectum. Examination of the genitalia was unremarkable except for a tiny, flat, smooth, lightly pigmented nevus on the dorsum of the shaft of the penis. (This lesion, together with similar ones on the left anterior shoulder and the medial aspects of both thighs and a keratotic lesion on the dorsum of the left hand, was excised subsequently.) There was a

*Accession No. S-2193, Fourth Army Medical Laboratory; and Accession No. 543896, Armed Forces Institute of Pathology.

†Accession No. 52-S-4351 and No. S-2609, Fourth Army Area Medical Laboratory.

10 cm., longitudinal, incisional scar over the outer aspect of the right lower-biceps region, extending to the flexion crease of the elbow joint. No evidence of persistent or recurrent melanoma was observed. There were no palpable right axillary lymph nodes. Reflexes were physiologic.

Laboratory studies performed on admission were reported as follows: red blood count 5.0 million; hemoglobin 14.4 Gm.; white blood count 9,250 with normal differential smear; urine clear, acid, with specific gravity of 1.023, negative for albumen and sugar, and microscopic examination of the sediment showing only an occasional white blood count per high-power field; corrected sedimentation rate 7; bleeding time 3½ minutes; clotting time 5 minutes; blood group O, Rh positive; and serologic flocculation tests 4 plus.

Roentgenograms of the chest, skull, and long bones were normal.

On Sept. 18, 1952, about five weeks after the original excision, axillary gland dissection was performed under Pentothal Sodium-nitrous oxide anesthesia. A curvilinear incision was made, beginning at the mid-point of the clavicle and curving downward and outward just inferior to the axillary hairline, to the posterior axillary fold at the level of the inferior angle of the scapula. Medial and lateral skin flaps were then developed, the lateral flap being carried to the region of the insertion of the pectoralis major muscle. The cephalic vein was identified and carefully cleared of areolar tissue, and the tendinous portion of the pectoralis major muscle was then isolated and divided by sharp dissection. The body of the muscle was then reflected medially, splitting the fibers inserting into the clavicle from the main portion of the muscle. The apex of the axilla was then identified between clavicle and first rib, and all areolar tissue was meticulously dissected from about the axillary vein, beginning at the lateral margin of the subclavius muscle. The medial and lateral anterior thoracic nerves and blood vessels to the pectoralis major muscle were carefully dissected free and preserved. As the dissection progressed laterally, the pectoralis minor muscle was isolated and transected about two inches proximal to the coracoid process. Here again, as the body of the muscle was reflected inferiorly its innervation and blood supply were carefully dissected free and preserved. Dissection was continued laterally along the axillary vein to a point well beyond the lateral margin of the latissimus dorsi muscle, preserving the long thoracic and thoracodorsal nerves and the subscapular vessels. En bloc removal of axillary node-bearing tissue was completed by carrying the dissection inferiorly along the free margin of the latissimus dorsi muscle and along the lateral thoracic wall, clearing the digitations of the serratus anterior muscle. Hemostasis was carefully secured with 0000 and 000 silk ligatures, after which the pectoralis minor and major muscles were reapproximated with a series of figure-of-eight sutures of No. 1 chromic catgut, reinforced with a continuous running suture of the same material in the fascia covering the pectoralis major muscle. A large Penrose sheath drain was inserted to the apex of the axilla, behind the muscles, and was brought out through the inferior angle of the incision. Subcutaneous tissues were then approximated with interrupted sutures of 0000 silk, and the skin was closed with interrupted, inverted mattress sutures of the same material. At no point during the dissection was a suspiciously enlarged or grossly involved lymph node encountered. Dry sterile dressings were applied, and a thick padding of sterile mechanics' waste was then padded in the axilla and applied tightly to the lateral thoracic wall by means of Elastoplast adhesive strips. The right arm was placed in a sling and was strapped in a modified Velpeau dressing with ACE bandages. The patient was given 500 c.c. of whole blood during the operation, and tolerated the procedure very well. Pathologic study of the specimen revealed no evidence of melanoma metastatic to the axillary lymph nodes.*

Postoperatively, the patient experienced relatively little discomfort, and exhibited a low-grade febrile response, with temperatures up to 100° F., for the first three days following surgery. He was placed on procaine penicillin 300,000 U. and dihydrostreptomycin 0.5 Gm. every six hours, prophylactically, but, on the eighth postoperative day, drainage, previously serosanguineous in character and only moderate in amount, became seropurulent and more profuse. Concomitantly, the patient noted increased discomfort in the anterior axillary fold,

*Accession No. 52-S-4665 and No. S-3042, Fourth Army Medical Laboratory.

particularly over the site where the pectoralis major muscle had been sutured. In this area, the skin became edematous, and reddened, and there was moderate tenderness to palpation. All skin sutures were removed, and the drainage was cultured, yielding an abundant growth of hemolytic *Staphylococcus aureus*, which, by sensitivity studies, was resistant to penicillin and Aureomycin, but moderately sensitive to terramycin, which was, accordingly, administered in doses of 0.5 Gm. every six hours. It was felt that the infecting organism may well have ascended through the drain, which was probably maintained in place for too long a period of time. The seropurulent drainage from the drain site gradually diminished, and the drain was progressively shortened and finally removed on Oct. 2, 1952. The reddened, edematous area overlying the pectoralis major suture line became fluctuant, and required daily aspirations, productive, on each occasion, of 5 to 10 c.c. of viscous, sanguinopurulent fluid, which, likewise, grew out hemolytic *Staphylococcus aureus* on culture. The combination of hot compresses and repeated aspirations, together with antibiotic therapy, served to quell the infection, so that, on Oct. 11, 1952, twenty-three days following surgery, the patient was discharged from the hospital entirely healed, but with some residual induration and adherence of the skin in the pectoralis major suture-line area. Because of this, he was able to abduct the arm only to a little over ninety degrees. At no time was there any edema of the right arm.

Fig. 1.

Fig. 2.

Fig. 1.—Normal abduction.
Fig. 2.—Hands in forceful apposition to show normal contraction of pectoralis major muscle.

During the ensuing weeks, the induration overlying the upper pectoralis major muscle gradually and progressively disappeared, and the skin in this area regained its mobility over pectoralis fascia so that, within two months of surgery, the patient had full right-shoulder motion (see Fig. 1). The pectoralis muscle group regained normal strength (see Fig. 2), and the patient volunteered that the right shoulder seemed as strong as it had been prior to surgery.

Comment.—This case illustrates the excellent functional result that can be obtained following axillary dissection with preservation of the pectoral muscles, without compromising the purpose of the operation. Furthermore, an excellent result was obtained in this case despite occurrence of a moderately virulent wound infection, a complication which, in retrospect, could probably have been prevented by performing dressings with the strictest, operating-room

sterile technique, at least until after the drain had been removed, and by removing the drain within the first three or four days. However, the end result in this case demonstrates that with proper selection of antibiotic a wound infection may be quelled so effectively that the classic postinfection fibrosis may be forestalled.

SUMMARY

1. Axillary gland dissection with preservation of the pectoral muscles for carcinoma of the upper extremity has been discussed, and certain criteria for the selection of cases for this procedure have been proposed.

2. The employment of this procedure as a prophylactic measure, following excision of a melanoma, and the ultimate good functional result are described.

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NONSIMULTANEOUS BILATERAL CARCINOMA OF THE BREAST

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THE occurrence of carcinoma in the remaining breast after radical removal of the first breast for cancer is a phenomenon familiar to most surgeons. For a number of years various men have discussed the question of whether or not the incidence of later carcinoma in the second breast is sufficiently great to warrant routine prophylactic removal of the contralateral breast at the time of treatment of the first carcinoma. Bloodgood[2] in 1921 and Pack[18] in 1951 have recommended such a procedure. However, as far as is known there are few emphatic proponents of such a practice today.

Certainly, in view of the shortcomings of present-day treatment, the removal of a breast before a cancer had arisen, or before it had produced clinical signs, would be the most effective means of conquering this disease. The worth of such a program would hinge upon a comparison of the number of lives saved and the mortality and morbidity (both physical and mental) incurred with such a procedure.

At the suggestion of Dr. Owen H. Wangensteen, a study of this problem has been carried out. It has consisted of two parts: first, a study of the incidence of nonsimultaneous bilateral breast cancer and, second, a study of the characteristics of patients with such bilateral cancers.

THE INCIDENCE FOUND CLINICALLY ON FOLLOW-UP EXAMINATION

Literature.—Although this study is primarily concerned with the problem of nonsimultaneous bilateral cancer, a review of the literature quite naturally finds both simultaneous and nonsimultaneous cases intermingled. William Nisbet[15] in 1800 described the case of a 40-year-old woman with simultaneous bilateral "cancer" of the breast. Velpeau[26] in 1938 wrote of excising the right breast, only to have a "scirrhous" tumor appear in the left breast shortly afterward. Since that time such case reports have been published quite frequently, and early textbooks speak of the clinical picture casually.

A number of series of breast cancer cases have been reported giving the incidence of bilateral cancer. Those series which have been described in more detail and which are more lucid are listed in Table I. Although these incidence rates appear somewhat comparable, nevertheless the author's criterion of true bilateral cancer varies in each series, and the exact length of follow-up is not given in any report.

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TABLE I. INCIDENCE OF CONSECUTIVE BILATERAL BREAST CANCER AS FOUND IN THE LITERATURE

AUTHOR	TOTAL CASES OF BREAST CANCER	NONSIMULTANEOUS BILATERAL CANCER	
		NUMBER OF CASES	PER CENT
Kilgore[12]	1100	13	1.17
Lewis and Rienhoff[13]	950	31	3.2
Harrington[11]	6361	212	3.4
Desaive[5]	1373	46	3.3

Presentation of Data.—

1. *Definition of terms:* In any discussion of multiple cancers, the immediate question arises as to the nature of the second tumor. Various criteria have been offered for deciding whether this second tumor is a new primary or a metastasis. Frequently quoted[9, 17] are Billroth's criteria, which are that each tumor must have a different histologic picture, that the tumors must arise in different locations, and that each tumor must produce its own metastases. As emphasized by Warren,[27] the latter stipulation is entirely too strict since many primary tumors treated today are without metastases. As related to bilateral breast carcinomas, it is also apparent that a difference or similarity in histologic configuration is of no significance. Any one breast carcinoma may vary markedly in any two microscopic fields and, on the other hand, two breast cancers, each from a different individual, may be indistinguishable under the microscope.

It has been shown anatomically that the lymphatics of the skin of the two mammary regions are continuous across the midline.[6, 20] Oelsner[16] also wrote of the demonstration of lymphatic collecting trunks extending from one mammary region to the supraclavicular region of the opposite side. Clinical evidence of these facts is seen not infrequently in multiple skin metastases extending across the midline or, occasionally, in metastatic carcinoma in the opposite axilla or supraclavicular region without apparent involvement of the adjoining breast. The possibilities of any tumor in the opposite breast being metastatic are, thus, always present.

It has been proposed that the second tumor is more apt to be a new primary if the interval between the appearance of the two cancers is longer. Although such a fact may be suggestive, none the less, metastases can occur after many years of quiescence and, conversely, it is certainly within the realms of possibility that a tumor occurring in the second breast after only a short interval may be a new primary.

Prolonged survival without metastases, after removal of the second breast, suggests strongly that the latter was a new tumor. Such was the situation in several of the cases to be presented later in this paper. Nevertheless, the occurrence of metastases shortly after, or concomitant with, the appearance of cancer in the second breast is by no means prima facie evidence that the second cancer is definitely metastatic.

There is little doubt that a varying percentage of breast cancers metastasize across the midline to the skin, breast, or opposite axilla. Such cases were estimated to be 3.2 per cent of the total breast cancers by Desaive,[5] and found to be 4.4 per cent of the total in our own series. Although one cannot be certain that such cases are metastases, such a likelihood is strong, as will be seen later

in the discussion, and it appears that such cases would not have been helped by a prophylactic simple mastectomy. In this regard may be mentioned the few autopsy series reported in the literature in which a relatively high percentage of bilateral cancers is reported. (Torok and Willelshofer,[24] 9 per cent; Gross,[7] 12.5 per cent.) Such series apparently include both simultaneous and nonsimultaneous cases, but in addition probably include a number of metastatic lesions across the midline. The details of such papers are not, however, sufficient to permit critical appraisal.

The original purpose in this work was to evaluate the thesis of prophylactic removal of the opposite breast when first confronted with a breast cancer. Since the question of metastasis versus a new primary cannot be answered definitely, it was felt that it would be better to include a few metastatic bilateral breast carcinomas, rather than to omit a few true bilateral primary tumors; for, although surgical aggressiveness in our approach to the cancer problem must be moderated, none the less, it is probably better to veer a bit to the radical side of the ideal rather than to the inactive side. On this basis, the only criterion used for calling a case bilateral carcinoma of the breast is microscopic evidence of such a tumor in both breasts.

Unless a statement is made to the contrary, the term "bilateral breast cancer" in the ensuing pages will refer to nonsimultaneous lesions.

2. *Material:* The case records were examined of all microscopically proved breast carcinomas in women which were reviewed in the Surgical Pathology Department of the University of Minnesota Hospitals from 1932 to 1939 inclusive. The records of four patients could not be found and these patients are not included. The remainder constitute 275 consecutive patients with a microscopically proved carcinoma of the breast. Three patients were first seen with simultaneous bilateral involvement of both breasts. These have been deleted, and henceforth the total will be considered as 272.

This study is not a complete one since not all patients have been followed to death. However, that it is a representative one is suggested by the fact that, of the 243 patients who have never developed a bilateral cancer while under observation, 50.6 per cent lived five years and 29.2 per cent lived ten years. There was one operative death, a transfusion reaction. One hundred seventy-four patients have been followed to death; 69 patients are still living, 59 after being followed for ten years or more, and 10 after being followed eight to nine years. Of these 69, nine patients were last seen with advanced metastatic disease, leaving 60 patients who might still ultimately develop a cancer in the other breast, of whom 40 are now under 70 years of age and 24 are now under 60 years of age.

3. *Results:* Of the 272 patients presenting with a cancer of one breast, 17 or 6.2 per cent were cases developing nonsimultaneous, microscopically proved, carcinoma in both breasts. Eight of these patients had had the first breast treated elsewhere and came to the University Hospital for treatment of the second breast. Nine patients presented with involvement of the first breast and developed carcinoma of the second breast during follow-up.

The microscopic slides of 22 of the bilateral cancers have been secured and the diagnosis of carcinoma confirmed. However, the slides of 12 tumors could not be found. The diagnoses in these cases are, with one exception, based upon the pathologic reports of staff pathologists at the University of Minnesota. In one case the diagnosis was made at a neighboring hospital by a pathologist who is considered capable.

There were, in addition, 12 other patients who developed gross carcinoma in the opposite breast, but who were treated only with radium and/or x-ray without biopsy. These have not been considered bilateral because the second breast tumor was not proved pathologically. As a matter of fact, the description of the lesions in most of these patients strongly suggested direct spread from the first breast. Eight of them had multiple skin metastases (unbiopsied), and the other 4 had massive distant metastases when the second breast tumor was discovered. None lived more than a few months after discovery of the second breast tumor. (Table II.)

It is apparent that the 8 patients who were first seen by us after having had one breast removed previously at another hospital represent a select group, since they were of the few among their sister patients at the place of treatment of the first cancer who lived long enough to develop the second cancer. Their presence at a university hospital might also be selective, since cancer in the second breast appears of unusual moment to most patients and to many physicians.

TABLE II. INCIDENCE OF NONSIMULTANEOUS BILATERAL BREAST CANCER IN UNIVERSITY OF MINNESOTA HOSPITALS SERIES

	NUMBER OF CASES	PER CENT
Total cases of breast cancer	272	100
Always unilateral	243	89.4
Bilateral, not biopsied	12	4.4
Bilateral, biopsied	17	6.2
a. Both done here	9	3.3
b. First done elsewhere	8	2.9

From the point of view of total risk incurred by any individual patient presenting herself with a unilateral carcinoma of the breast, a clearer picture is seen, therefore, if one ignores these 8 cases and calculates the incidence of nonsimultaneous bilateral breast carcinoma in the 264 patients who presented themselves with carcinoma in the first breast. Thus of 264 patients, 9 (3.4 per cent) developed microscopically proved carcinoma of the opposite breast during follow-up, and 12 developed clinically apparent, but unbiopsied, carcinoma of the opposite breast, the latter cases strongly suggesting a metastatic origin. Such a calculation is necessary in that it takes into consideration the patients who die shortly after operation and thus, from a practical viewpoint, are not concerned with this problem.

4. *Comparison with the general population:* In an effort to offer a base line with which future incidences may be compared, we have utilized the factor, "risk years" of observation, as suggested by Warren.[28] We have calculated the total number of years of observation of those 264 patients seen by us with

their first cancer. The follow-up in the bilateral cases is computed only up to the development of the second tumor, ranging from nine months to nine years. Thus, during a total of 1540.5 years of observation, cancers developed in the opposite breast in nine patients, an average of 5.8 cancers per 1,000 patient-years of observation.

As a control group, the total number of cases of breast carcinoma reported to the Connecticut State Cancer Registry for the years 1935 to 1946 was divided by twelve.[14] This number, which has been classified according to age, we have assumed as a yearly occurrence rate. From the United States census for the female population of Connecticut, according to age, for the year 1940,[21] we have then computed the yearly incidence of breast carcinoma for the various age groups. From the point of view of period of observation, our cases likewise were observed mainly over the period from 1935 to 1946. From this standpoint, then, the two groups are fairly comparable. The difference in geography has been necessarily ignored. Although by no means a perfect control group, the extensive labors of the Connecticut Cancer Registry appear to present as complete a picture of cancer incidence as is available today.

The patients have been divided into two broad age groups. Our patients who developed the first cancer before the age of 50 years have been compared with the Connecticut population of 30 to 60 years, since these cases were followed for a total of 628 patient-years, all of which involved this same age span except for a total of 5.5 years of observation over 59 years of age. Those patients developing cancers after 50 years have been compared with the Connecticut population of 50 years and above, since the period of observation of these patients covered the ages of 50 to 94 years.

As seen in Table III, those patients developing the first cancer before the age of 50 years showed an incidence of cancer in the second breast which was significantly greater than the incidence of breast cancer in the population at large, there being less than one chance in twenty that such a difference would have occurred by chance. On the other hand (based upon the principle of X^2), there was no significant increase in cancer of the second breast when the patient developed the first cancer after the age of 50 years.

In any discussion of prophylactic surgery for cancer, the question arises as to whether removal of any one organ would be more fruitful than removal of another. It is therefore of interest that the 264 patients, seen with their first

TABLE III. BREAST CANCERS DEVELOPED PER 1,000 RISK YEARS BY CASES WITH PREVIOUS UNILATERAL BREAST CANCER* AND BY THE GENERAL POPULATION OF CONNECTICUT

	CANCERS PER 1,000 RISK YEARS		
	ALL AGES	30 TO 60 YEARS	OVER 50 YEARS
University of Minnesota breast cancer series	5.8	6.3	5.4
Connecticut population	0.84	0.65	1.2
	$X^2 = 4.517$ $P = < 0.05$	$X^2 = 4.573$ $P = < 0.05$	$X^2 = 2.58$ $P = > 0.10$

*Reviewed at the University of Minnesota Hospitals.

breast cancer, developed 18 cancers during follow-up. Nine (50 per cent) of these were breast cancers, and 9 were situated in other organs (3 uterine, 1 ovarian, 1 gastric, 1 of the tongue, 2 of the skin, and 1 sarcoma of the soft tissue). This percentage of breast cancers, 50 per cent, contrasts with the relative incidence of breast cancer in Connecticut, 29 per cent of all cancers of women, 30 to 80 years of age.

THE OCCURRENCE OF UNSUSPECTED CANCER IN THE REMAINING BREAST WHEN THE LATTER IS REMOVED PROPHYLACTICALLY

Since March, 1950, a study has been carried out at the University of Minnesota Hospitals in which the asymptomatic remaining breast has been removed prophylactically by simple mastectomy in patients who have already had one breast excised radically for a known cancer.

Material and Methods.—The patients have been selected to include principally those in the younger age groups. Thus, of the 16 patients studied, only 3 have been over 50 years of age at the time of removal of the remaining breast. Three of them had had a close relative with breast cancer. In other respects they were characterized only by having a treated, microscopically proved cancer of one breast and a remaining breast which presented no clinical abnormality.

Of the 16 breasts, 6 have been examined in a routine manner. Thus, the breast has been sectioned by hand at approximately 1.0 cm. intervals, and the breast tissue has been examined grossly by sight and palpation, sections being taken of representative areas including those which stood out due to a difference in consistency or color.

The remaining 10 breasts have been examined more thoroughly, the whole cross section of the breast being examined microscopically at intervals of 1.0 cm. or less. Individual blocks were cut larger than is customary so that the finished sections measured 2.5 to 4.5 cm. in diameter. This procedure produced from 40 to 200 sections per breast depending upon the size of the breast.

Results.—Of the 16 breasts removed prophylactically, small cancers, not detected clinically, were found in two. A brief summary of these 2 cases is as follows:

CASE 1 (University Hospitals No. 785192).—Mrs. M. U., a 32-year-old white woman, underwent a right radical mastectomy on Jan. 23, 1948, for a scirrhous carcinoma lateral to the nipple with axillary lymph node metastases (Fig. 1). On March 22, 1950, the asymptomatic left breast was removed by simple mastectomy. Random microscopic sections revealed a minute focus of scirrhous carcinoma, the size of one low-power field (Fig. 2, *A.*). Radical excision of the left pectoral muscles and axillary contents was performed on June 16, 1950. However, the patient expired on March 9, 1951, with extensive skeletal metastases.

The presence of tumor in lymphatic vessels (Fig. 2, *B.*) suggests that the second tumor may have been metastatic. However, as discussed previously, one cannot be certain that this cancer was not a new primary.

CASE 2 (University Hospitals No. 807336).—Mrs. B. W., a 46-year-old white woman, underwent radical mastectomy of the left breast on Dec. 16, 1949, for a carcinoma beneath the left nipple with axillary node involvement (Fig. 3). On May 25, 1950, the asymptomatic right breast was removed. Multiple microscopic sections revealed two small areas of cancer, one scirrhous (Fig. 4) and one medullary (Fig. 5). Radical mastectomy was completed on June 7, 1950, and the patient is living and well at the present time.

ANALYSIS OF PATIENTS WITH NONSIMULTANEOUS BILATERAL BREAST CANCER

To the 17 cases of nonsimultaneous bilateral carcinoma found in our 1932 to 1939 series, we have added 9 cases that occurred among hospital admissions since 1939. This total of 26 consecutive cases has been analyzed from various standpoints.

Location.—In only 1 case were both cancers in the medial quadrants of the breast. In 7 cases either the first or second cancer was in a medial quadrant, but the contralateral cancer was then in either the lateral hemisphere or in the nipple line.

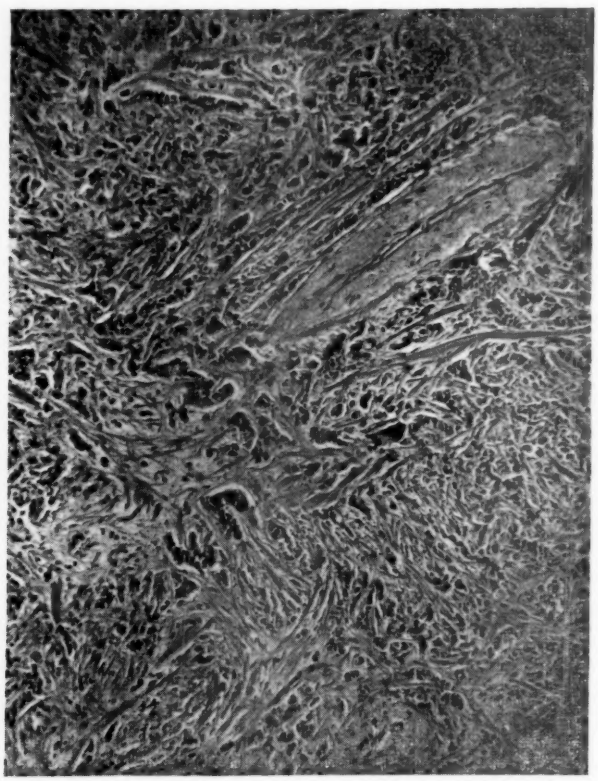

Fig. 1.—Microscopic view of the cancer in the first breast (right) of the patient, M. U.

Since location in the medial quadrants might be suspected as evidence of metastasis rather than of a new primary, it is of interest that the one patient with two medial tumors is living and well seventeen years after the second mastectomy.

Interval.—The interval between the occurrence of carcinoma in the two breasts varied from four weeks to thirty-two years, the second cancer occurring within five years or less in 16 cases, and within ten years in 22 cases. There was no apparent relationship between the length of the interval and survival after the second cancer.

Node Involvement and Survival.—In relation to the first breast, there was axillary node involvement in 12 cases and no node involvement in 6 cases. In

regard to the second breast, there was no node involvement detected in 10 cases and positive node involvement in 9 cases. In the remainder, the nodes were either not described or were not sectioned, or only a simple mastectomy was performed.

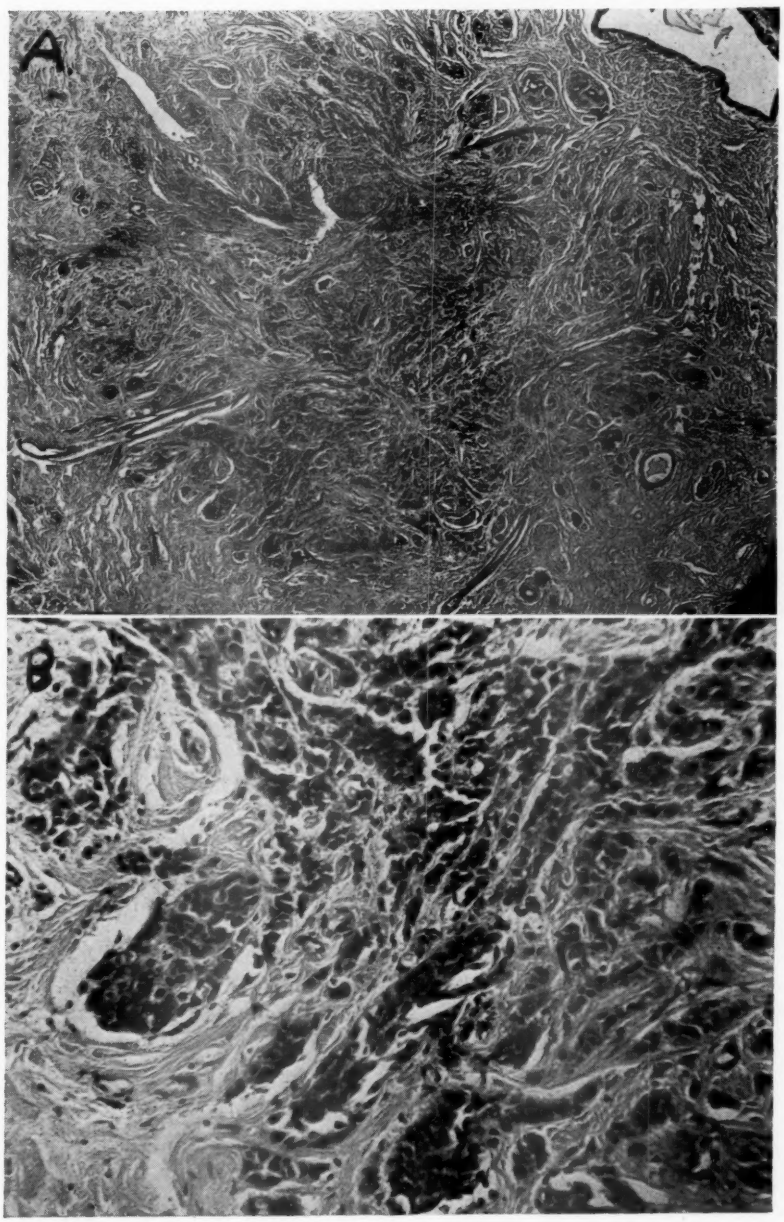

Fig. 2.—The cancer in the second breast (left) of the patient, M. U. *A*, Low magnification showing cross section of the entire tumor; *B*, higher magnification.

As would be expected, the survival time following the first cancer was unusually long. Twenty-three patients had had their first cancer removed five or more years before, and 19 (82.6 per cent) of these survived five years after

the first cancer. Of those whose first cancer was removed ten or more years before, there were 20, of whom 15 (75 per cent) lived ten years.

The whole group presents an average survival time of 5.3 years from time of operation on the second breast. Twenty patients had the second mastectomy five or more years before and, of these, 11 (55 per cent) lived five years. Such a survival rate suggests that the lesions in the latter patients were separate primaries rather than metastases.

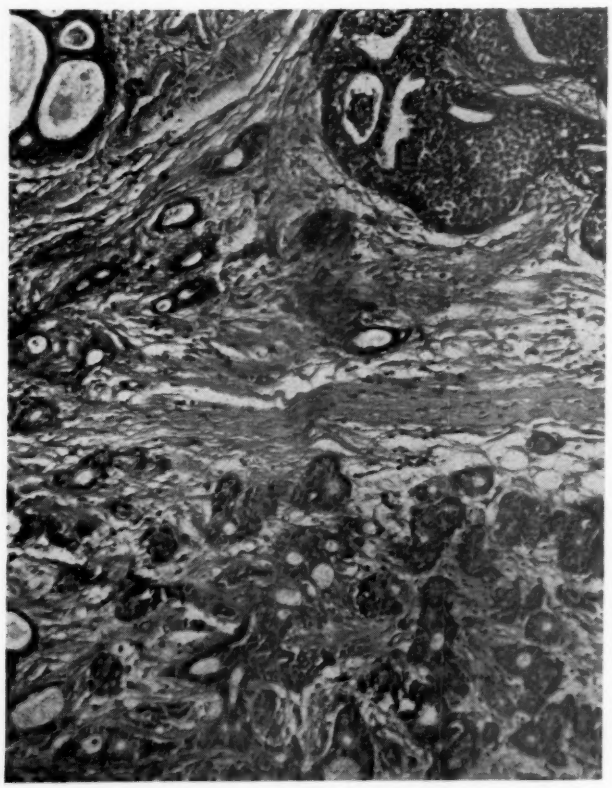

Fig. 3.—Microscopic view of the cancer of the first breast (left) of the patient, B. W.

Age Distribution.—Regarding actual yearly risk of developing a second cancer, no significant difference was found between those patients developing the first cancer at an earlier age and those developing the first cancer at a later age (Table III). However, among the patients with bilateral cancer, 61.5 per cent developed the first cancer before the age of 50 years, compared to 39.5 per cent of the 243 patients with unilateral cancer in the original series. This latter finding coincides with those of Desaive,[5] and may be explained by the fact that younger patients are the ones who live long enough to develop a second cancer, though year for year their risk does not seem to be greater.

Menopause.—The age differences just discussed are also reflected in the relationship of cancer occurrence to the menopause.

Of the 15 bilateral patients developing the first cancer before the menopause, none were sterilized. However, of the 82 patients who developed uni-

lateral cancers before the menopause, only 18 were sterilized, so this finding is of little significance alone.

Tumor Types.—Comparison of the bilateral cancers and 45 cancers which had remained unilateral for at least nine years revealed no significant histologic differences. The usual cancer types were found with the usual distribution.

Adenocystic Disease.—From the point of view of clinical evaluation, in only one of the 26 patients was the first breast noted to contain other masses or

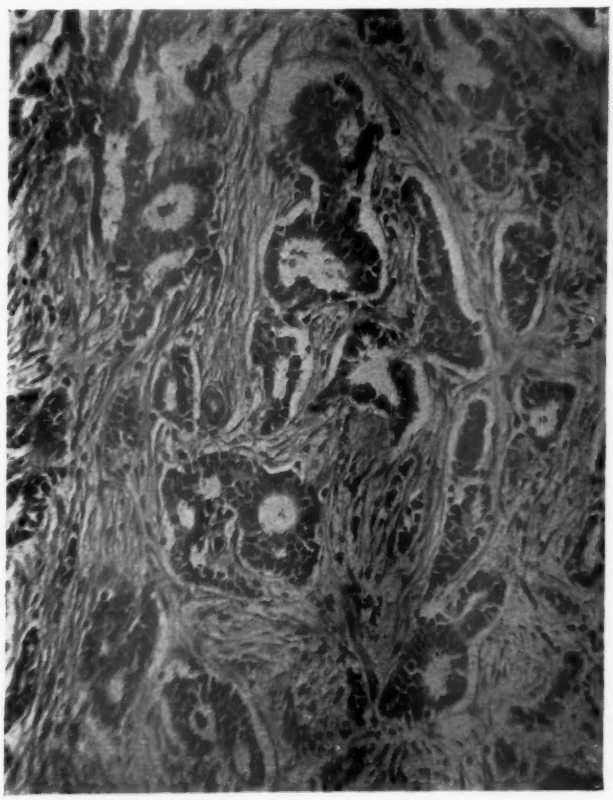

Fig. 4.—Microscopic view of the scirrhous cancer in the second breast (right) of the patient, B. W.

cysts, or was it described in any way that would suggest the presence of adenocystic disease. The second breast (that is, the breast which later developed the second tumor) was described in a similar fashion in only 3 cases. In only 1 case were both the first and the second breasts described as involved. This case, included in the previously mentioned listing, was also the only case in which the cystic disease was described as "massive, involving the whole breast." (The patient also gave a history of breast cancer in two maternal cousins. *Vide infra.*)

Regarding microscopic adenocystic disease, no difference was found between those breasts with bilateral or unilateral cancer, although not enough sections were taken of each breast to be conclusive in regard to this point.

Sterility.—All the patients with bilateral cancer were married, 2 being nulliparous and 24 patients having an average of 2.7 children, findings quite comparable to those patients with unilateral cancer.

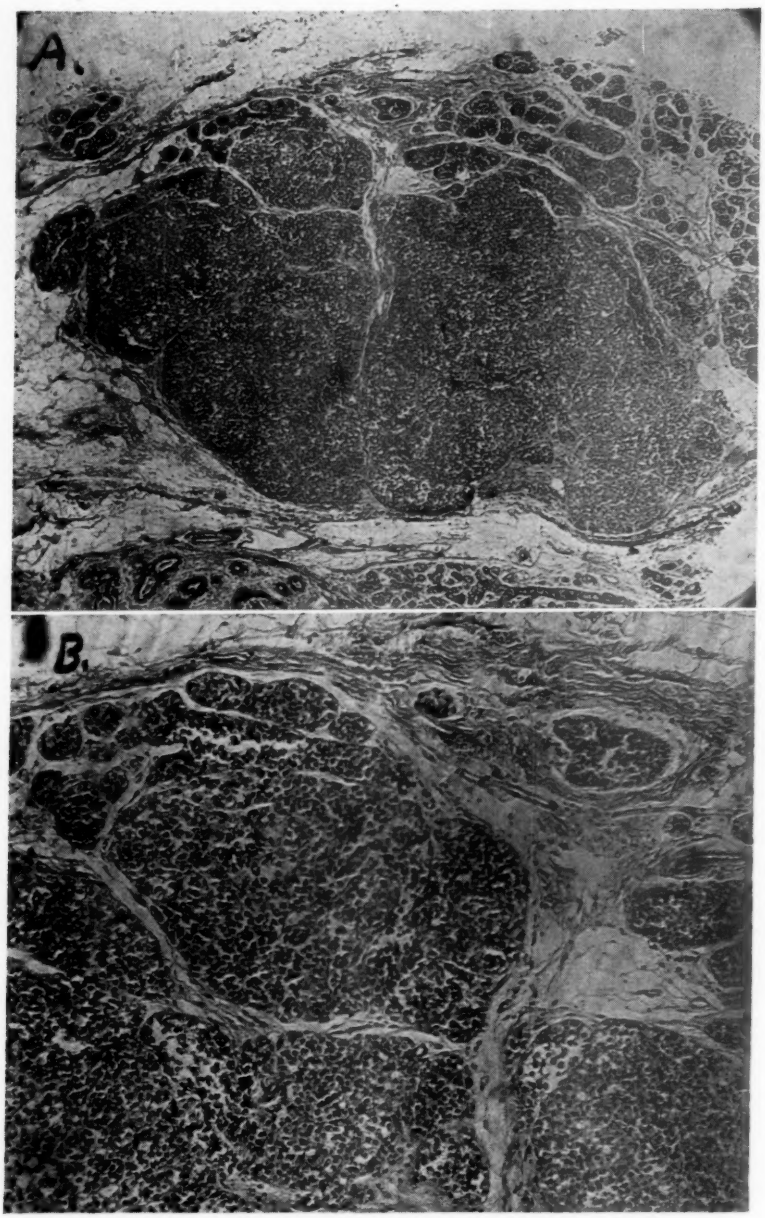

Fig. 5.—Microscopic view of the medullary cancer in the second breast (right) of patient, B. W. *A*, Low magnification (×30) showing a cross section of the entire tumor; *B*, higher magnification (×100).

The Influence of Pregnancy After the First Cancer.—

1. *Literature:* Brooks and Proffitt[4] have recently concluded that there is no evidence that pregnancy is influential in originating breast cancer; and, therefore, that, if a unilateral breast cancer is completely extirpated, pregnancy

can be permitted without fear for the other breast. They reported 5 patients who became pregnant after operative removal of a cancer of one breast. None of these developed a carcinoma of the opposite breast. However, it should be noted that the one patient who had been followed for five years after pregnancy had an original lesion, the malignancy of which was in dispute. Of the other 4 patients, 1 died two months after delivery, 1 was pregnant at the time of writing, and the other 2 had been followed two months and one year, respectively.

In 1949, Steffen and Grace[23] presented 4 cases of patients who became pregnant after a unilateral breast cancer and who had not developed a contralateral cancer. These patients had been followed for eight years, two years, three years, and four months, respectively, the latter patient dying at the time of metastases.

In 1937, Smith[22] described 9 patients who became pregnant after a breast cancer had been treated. These patients had been followed from four months to six years after pregnancy. No mention or discussion was made by the author regarding the opposite breast, the paper dealing only with the effect of pregnancy on existing cancer (*vide infra*).

Also in 1937, Harrington[10] presented a series of 45 patients who became pregnant after treatment of a breast cancer and who were followed for known periods after the pregnancy. (Only 37 patients went to full term.) Following pregnancy, 30 patients had lived at least three years, 28 had lived at least five years, 14 at least ten years, and 8 had lived at least fifteen years. Like the preceding paper of Smith, Harrington was interested only in survival in relation to the first cancer. Therefore, although none of the previously mentioned patients (presented only in tabular form) was described as developing a cancer in the opposite breast, one cannot be certain that this was so. Thus Harrington also presented 5 cases in some detail of patients who had been pregnant at the time of the first cancer and who had also had another pregnancy after treatment of the latter. In the case history of 1 of these 5 patients, it was mentioned in passing that the patient had had the remaining breast amputated for cancer ten months after the second birth. Thus, of the only 5 detailed case histories given, one patient (20 per cent) developed a cancer of the opposite breast. The absolute lack of emphasis or further discussion of the point leads me to accept with reluctance the definite conclusion that none of the previously described 45 patients had developed a contralateral cancer, in the absence of an excluding statement in this regard by Harrington, for it is well known that the apparent frequency of any disease process is directly proportional to an individual's interest in that disease. Thus, although it would seem apparent from the foregoing pages that carcinoma of the remaining breast is by no means infrequent, nevertheless there are numerous follow-up studies of large numbers of breast cancer patients in the literature which make absolutely no mention of bilateral cancers, and from which one might make the casual observation that no such cases had occurred.

Trout,[25] in 1921, reported 31 cases of breast carcinoma in patients who were below 40 years of age. Two of these patients became pregnant after treatment

of the first breast. Both patients developed carcinoma of the opposite breast during or following pregnancy, although in only 1 case was the second tumor examined microscopically. Trout also wrote to a number of physicians, and received reports of 15 cases where pregnancy had occurred after a primary breast carcinoma was removed. Thirteen of these patients subsequently developed carcinoma in the opposite breast, there ensuing from two to ten years between the first breast cancer and the pregnancy.

Heinz Bromeis[3] more recently reported upon 14 patients in whom pregnancy occurred immediately after, or several years after, radical mastectomy for cancer. In 6 of these patients a carcinoma developed in the opposite breast following pregnancy, the tumors appearing to be new primaries as far as he could determine.

Of the 46 cases of nonsimultaneous bilateral breast carcinoma reported by Desaive,[5] there were 2 cases in which he observed "the coincidence of a pregnancy and the development of a cancer in the second breast."

2. *Presentation of data:* Our material adds little to these findings. However, it is interesting that 1 of our 26 patients developed the first breast cancer in 1944, at the age of 37 years, had two children in 1946 and 1948, respectively, and developed a carcinoma of the opposite breast in 1951 (O. R., University Hospitals, No. 746973).

3. *Discussion:* This evidence is, of course, not conclusive. However, since it is rather rare for a patient to become pregnant after having had a breast cancer, the incidental occurrence of such cases in the small series of Desaive and the present writer is certainly suggestive. Nor can the high incidence of bilateral carcinoma in the reported cases of Trout and of Bromeis be ignored. The evidence available, that pregnancy is rarely followed by cancer in the opposite breast, suffers either from brevity of follow-up and smallness of numbers, or from the fact that absence of such contralateral cancers was not specifically denied by the respective authors whose papers dealt with other aspects of the disease.

For the foregoing reasons, I believe that, until more evidence is presented to the contrary, pregnancy should not be permitted following apparent "cure" of a breast cancer, unless the opposite breast is first removed prophylactically by simple mastectomy.

The Influence of Heredity.—

1. *Literature:* Handley,[8] in 1938, told of a family of 5 sisters of whom 2 had bilateral carcinoma of the breast, 1 had an unbiopsied unilateral carcinoma of the breast, 1 had both breasts amputated for "proliferative mastitis," and the fifth had x-ray and radium treatment for "mastitic induration."

Wood and Darling,[29] in 1943, reported an incomplete pedigree of 4 generations of 1 family. There were 4 cases of bilateral breast carcinoma. In the third generation all 3 sisters had breast cancer, 2 bilateral and 1 unilateral.

Such reports are of interest, for, although the exact significance of heredity in human breast cancer is not known today, one might expect both breasts to be affected if such a factor were at play.

2. *Presentation of data:*

(a) Material: A family has recently been called to our attention in which there are 6 sisters, of whom 5 have had breast cancer, 2 bilateral and a third probably bilateral. However, such individual case reports, while suggestive, are none the less inconclusive. An effort has been made, therefore, to find out how many of our 26 patients with bilateral breast cancer present a family history of the disease. The latter findings have been compared with the pedigrees of a group of patients with unilateral breast cancers.

As a control group, 360 consecutive cases of breast cancer were studied from the files of the Dight Institute. The latter, under the direction of Dr. Sheldon Reed, is carrying out a thorough survey of the family histories of patients with breast cancer.[19] The cases consist of patients with breast cancer seen in the Tumor Clinic of the University of Minnesota Hospitals, and thus are quite comparable to ours in background and environment; indeed, many of our cases appear in the Dight Institute files. The age distribution of the patients in the latter group is comparable to that of the patients with unilateral breast cancers in our own series.[1]

Both in our bilateral cancers and in the Dight Institute cases, family histories have been obtained by personal interview or correspondence with the patient and/or as many relatives as possible. Most reported cases of cancer in relatives have been confirmed by either the death certificate, the pathologic report, or a letter from the attending physician. Where a cancer is unconfirmed but is listed as "probable," its occurrence has been alleged to by usually more than one relative with apparent certainty.

Of the 360 Dight Institute cases, 6 were bilateral cancers, and in 54 cases completely negative progress had been made in investigating the family histories. These 60 cases have, therefore, been deleted, leaving 300 cases of unilateral breast cancer as a control group. Of our 26 patients with bilateral cancers, there were 2 cases in which the fate of the patient's family is unknown and untraceable due to their location behind the Iron Curtain. Therefore, these 2 cases have been deleted, leaving a total of 24 patients with bilateral cancers in the ensuing discussion.

In neither our 24 cases nor the pedigrees of the Dight Institute is the information felt to be sufficiently complete to compare all members of the family. The information regarding mothers and sisters, however, is felt to be sufficiently reliable to allow for statistical analysis.

(b) Results: Of the 24 patients with bilateral breast cancers, 11 had a mother or sister with carcinoma of the breast (10 proved, 1 probable but unconfirmed). Of the 300 patients with unilateral breast cancer, 27 had a mother or sister with breast cancer (24 confirmed, 3 probable but unconfirmed). This difference in incidence, 45.8 per 100 as compared to 9.0 per 100, is striking. However, there is a possible fallacy in that the number of the sisters and their ages could influence such results considerably. Therefore, the sisters have been segregated according to age. Only those sisters have been considered who have either developed a breast cancer already, or who have reached the age of 60 years (Table IV).

Among the bilateral cancer patients there were 28 sisters at least 60 years of age or with breast cancer. Of these 28, there were 6 breast cancers (21.4 per cent). Among the patients with unilateral cancer there were 318 sisters at least 60 years of age or with breast cancer, of whom 22 (6.8 per cent) had breast cancer ($X^2 = 5.46$; $p = <0.02$).

TABLE IV. THE FAMILY HISTORY IN REGARD TO BREAST CANCER IN MOTHERS AND SISTERS OF PATIENTS WITH UNILATERAL AND BILATERAL BREAST CARCINOMA

	TOTAL MOTHERS	MOTHERS WITH BREAST CANCER		TOTAL SISTERS 60 YR. OF AGE OR WITH BREAST CANCER	SISTERS WITH BREAST CANCER	
		CASES	PER CENT		CASES	PER CENT
Bilateral cancers	24	6	25.0	28	6	21.4
Unilateral cancers	300	9	3.0	318	22	6.8
		$X^2 = 24.64$ $P = < 0.001$			$X^2 = 5.46$ $P = < 0.02$	

Six of the 24 mothers in the bilateral group developed breast cancer (25 per cent), while in the unilateral group, 9 of 300 mothers developed breast cancers (3 per cent) ($X^2 = 24.64$; $P = <0.001$) (Table IV).

Among the sisters of the bilateral patients, there were 7 with cancer. It is striking that 6 of these cancers were of the breast and 1 was unspecified, being called "generalized carcinomatosis." Based on the 29 sisters who had reached the age of 60 years or who had developed any kind of cancer, there was, then, one sister with cancer other than breast cancer, or 3.4 per cent. Among the sisters of the unilateral cancer patients, there were 355 who had reached the age of 60 years or who had cancer of any kind. Thirty-seven (10.4 per cent) of these sisters developed cancer other than breast cancer.

Of the 24 mothers of the patients with bilateral cancer, 12 (50 per cent) developed cancer of some kind, as compared to 15 per cent of the mothers of the patients with unilateral cancer. However, if one deletes the breast cancers, there is not then a significant difference in the incidence of cancers other than in the breast (25 per cent of mothers in the bilateral cases, 12 per cent of mothers in the unilateral cases) ($X^2 = 3.33$; $P = >0.05$).

As previously stated, records are not felt to be complete with regard to more distant members of the family. However, it is of interest that of the 24 bilateral cancer patients, 15 (62.5 per cent) showed a family history of breast cancer in any relative. Of these 15, 3 gave a family history of bilateral cancer, and 2 had more than one relative with breast cancer. This proportion (62.5 per cent) contrasts with the unilateral cancer patients, who gave a family history of breast cancer in any relative in 46 cases (15.3 per cent).

The incidence of cancer in male relatives was similar in both unilateral and bilateral groups.

These findings suggest strongly that patients with bilateral breast carcinoma show an increase in breast cancer among their relatives, especially in regard to

mothers and sisters. One might infer that the patient who presents herself with a first breast cancer and with a family history of breast cancer suffers a greater risk of developing cancer in the opposite breast.

It is interesting in this regard that, of the total 306 Dight Institute patients whose pedigrees had been investigated, there were 52 patients who gave a family history of breast cancer. Six (11.5 per cent) of these were nonsimultaneous bilateral cancers. The 52 patients had been followed for an average of 5.6 years, with an incidence of 20.4 cancers in the opposite breast per 1,000 risk years. This incidence contrasts markedly with that in our original series. The comparison assumes added significance if one considers that the latter cases included patients both with and without a positive family history of breast cancer.

DISCUSSION

Prophylactic simple mastectomy of the asymptomatic remaining breast was performed on 16 patients with unilateral cancer. In 2 cases, minute carcinomas were found in this remaining breast. Such an incidence would certainly imply that nonsimultaneous bilateral cancer is frequent enough to be always considered when treating patients with breast cancer. However, this series is too small to permit any conclusions regarding absolute incidence, for the occurrence of only 2 cancers may well have been fortuitous. A larger group of 264 patients has revealed on thorough follow-up an incidence of nonsimultaneous bilateral cancer of only 3.4 per cent, and this percentage is compatible with other reported incidences in the literature.

It is evident that a woman from whom one breast has been removed has already fallen from her pedestal of perfection and that, therefore, removal of the remaining breast should appear as less of a loss than if she were in her original intact state. It is also apparent that a chest is more symmetrical, and that a prosthesis is more satisfactorily fitted and worn, if both breasts are absent rather than only one. However, one rarely has a patient with a single breast removed spontaneously ask one to remove the other for cosmetic purposes. The allegiance of a woman to her remaining breast is incalculable and variable; and there is some doubt that a risk, thus far shown to be only 3 to 4 per cent, is sufficient to predicate the indiscriminate urging of prophylactic simple mastectomy of the opposite breast for all patients with breast cancer. As a matter of fact, the risk of death is somewhat less than 3 to 4 per cent, since 55 per cent of our patients lived five years after removal of the second carcinoma.

None the less, the fact remains that some patients do develop a second cancer and some of these latter patients undoubtedly succumb to the second tumor after cure of the first. An analysis of patients with nonsimultaneous bilateral breast cancer, to find some characteristic which would apply to only a small segment of those women presenting themselves with the first cancer and which would nevertheless allow one to prognosticate the future development of a cancer in the remaining breast, has revealed only two points. These are as follows: (1) Patients with bilateral cancer have a family history of breast cancer in a large proportion of cases in contrast to those with unilateral cancer;

and, conversely, a small group of breast cancer patients with such a positive family history showed an unusually high incidence of bilateral carcinoma. (2) There is some admittedly empirical, but none the less striking, evidence that pregnancy after a first breast cancer may predispose to cancer of the other breast.

This analysis has been based upon only 26 cases, obviously too small a number for any didactic conclusions. However, from a practical point of view, the inferences appear strong enough to warrant the following program: When a patient presents herself with an operable breast cancer, prophylactic simple mastectomy of the opposite breast should be urged for (1) that patient who has a family history of breast cancer and (2) that patient who is premenopausal and who desires to have children after the first cancer is apparently cured.

The removal of these two groups would make the risk expected by the remaining patients even less, and it is suggested that the latter be handled by careful follow-up examinations of the remaining breast by patient and doctor without prophylactic mastectomy of the opposite breast.

SUMMARY

1. When a woman has had a cancer of one breast, the risk of cancer in the opposite breast is a significant one that cannot be ignored.

2. As evidence of this, the prophylactic removal of the asymptomatic opposite breast in patients with one breast cancer has revealed minute unsuspected cancers in 2 of 16 cases.

3. A follow-up study of patients operated upon for carcinoma of the breast at least ten years before reveals an incidence of nonsimultaneous bilateral cancer of 3.4 per cent.

4. This incidence is greater than that found in the population at large with regard to women under 50 years of age at the time of the first cancer, but not with regard to women over 50 years of age at the time of the first cancer.

5. Age distribution shows a slight shift to the younger age groups in bilateral cancers, compared to unilateral cancers. However, per unit of time, younger women have not been shown to undergo a significantly greater risk than those who are older.

6. The rather satisfactory survival rate after the second cancer suggests that many of the latter are true second primaries.

7. Patients with bilateral breast cancer show no unique characteristics in regard to the location of the tumors, axillary node involvement, sexual history, tumor type, or benign breast pathology.

8. There is some strongly suggestive, though inconclusive, evidence that pregnancy after a single breast cancer may predispose to cancer in the other breast.

9. Patients with bilateral cancer appear to have a significantly greater number of mothers and sisters with breast cancer than do those with unilateral carcinoma.

10. Prophylactic simple mastectomy of the opposite breast is recommended for those patients who have an operable breast cancer and who (a) have a family history of breast cancer or (b) are premenopausal and desire to become pregnant.

11. All other patients with unilateral breast cancer, not included in these two groups, should not have a routine prophylactic simple mastectomy, but should be followed carefully with frequent examinations of the remaining breast.

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THE CHOLESCINTIGRAM

A Preliminary Report

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THE "cholescintigram" is a new technique for the visualization of the gall bladder. The method employs intravenous radioactive diiodofluorescein (DIF) as the tracer agent and the directional scintillation counter to record the gamma radiation. This technique was developed for use in the many situations in which oral cholecystography is not feasible. The cholescintigram embodies most of the advantages of intravenous cholecystography without its deleterious toxic effects.

METHOD AND MATERIAL

Diiodofluorescein (I^{131}) was chosen as the tracer agent because it rapidly concentrates in the gall bladder. It has been used extensively in other investigations[5] and has been without toxic effects when used in the dosages required by radioactivity surveys. Iodine^{131} has the advantage of a short half life (eight days) and a gamma radiation sufficiently intense to be recorded externally by the scintillation counter.[3] The scintiscanner (see Fig. 1) is used to record visually the radioactivity detected by the counter. This instrumentation has been described in a previous publication.[1]

In preliminary experiments on animals it was determined that a dose of DIF of 10 to 15 μc. per kilogram of body weight resulted in satisfactory concentration in the gall bladder. The radio dye appeared twenty to thirty minutes after injection, reached a maximum at one hour, and disappeared in four hours.

Accordingly then, 1 mc. of DIF (I^{131}) is administered to the patient intravenously. Approximately twenty minutes after injection, the patient is placed supine on an ordinary examining table. An area extending from the right flank to the midline and three inches above and below the right costal margin is marked on the patient's skin. The counter is then set to survey this area, and scanning is begun. For an average patient, the survey is completed in twenty minutes. Scanning is performed at intervals of twenty minutes, one hour, and two hours after injection. In those cases where no concentration of DIF has been observed at the end of two hours, the survey has been repeated as long as four hours after injection in order to confirm this observation.

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RESULTS

The optimal dosage and the appearance and disappearance rates of the DIF were determined in experiments initially performed on rabbits and dogs. The radio dye was found to appear in the liver within ten minutes after intravenous injection, but did not appear in the gall bladder in any significant concentration until twenty minutes after administration. The concentration in the gall bladder reached its maximum thirty to forty minutes after injection. It was also observed that during this period the hepatic concentration was decreasing and that scanning at this time yielded the sharpest delineation of the gall bladder. Thereafter, the gall bladder concentration progressively decreased until, after four hours, only a trace of radioactivity could be detected.

Quantities of the tracer agent varying from 1 to 20 μc. per kilogram of body weight were used, and it was found that a dose of at least 10 μc. per kilogram was necessary for obtaining satisfactory visualization of the gall bladder in the experimental animal. As the dosage was increased up to 20 μc. per kilogram, sharper delineation of the gall bladder was observed.

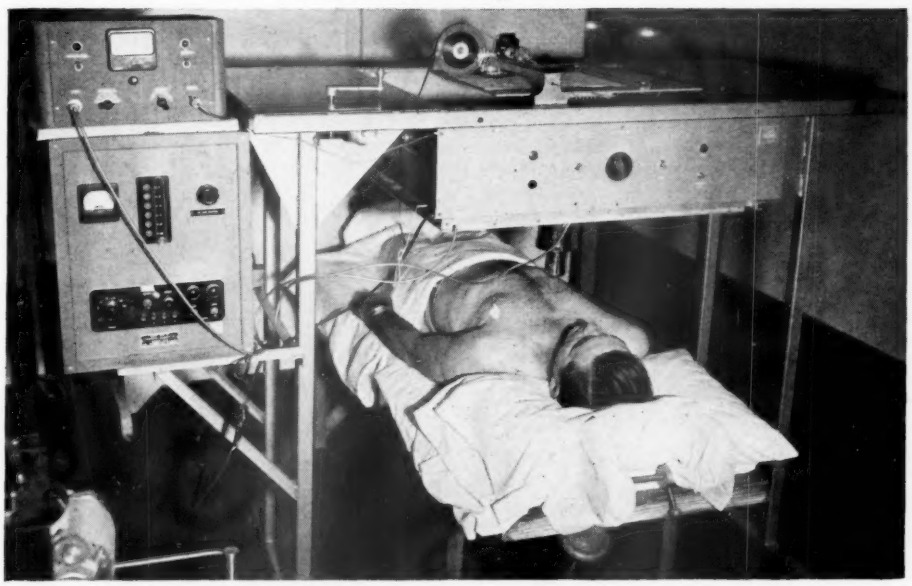

Fig. 1.—The scintiscanner with the scintillation counter in position for scanning the area of the gall bladder.

Three animals were sacrificed thirty to sixty minutes after injection. The liver and gall bladder were removed and in vitro scanning was performed (see Fig. 2). The gall bladder was then carefully removed from each of these preparations in such a manner as to avoid spillage of bile, and the scintigram was repeated (see Fig. 3). The first scintigram showed a sharp focus of radioactivity closely corresponding to the anatomic size and position of the gall bladder (see Fig. 2). In the scintigram performed after removal of the gall bladder (see Fig. 3), this focus of radioactivity was not present. These observations demonstrated that the focus of radioactivity was due solely to concentration of the DIF within the gall bladder.

Upon completion of these experiments, the technique was applied to ten patients. Six of these had been demonstrated by routine oral cholecystography to have normal gall bladder function. The cholescintigram in each of these patients revealed an area of concentrated radioactivity in the right upper

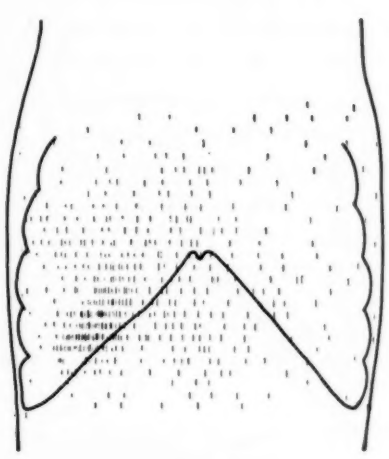

Fig. 2.

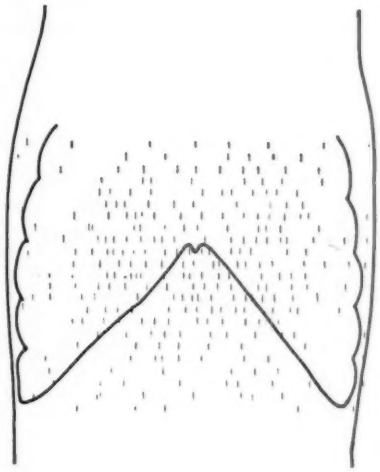

Fig. 3.

Fig. 2.—Scintigram of a liver-gall bladder preparation of the rabbit. Note the sharp focus of radioactivity at the right mid-costal margin.

Fig. 3.—Scintigram of the liver preparation illustrated in Fig. 2 performed after the gall bladder was excised. Note that there is no focus of radioactivity.

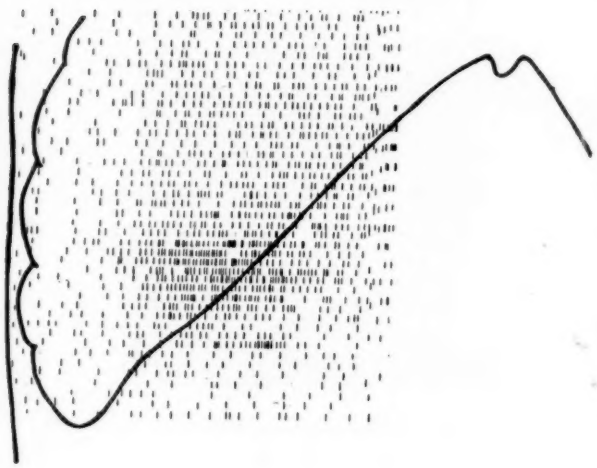

Fig. 4.

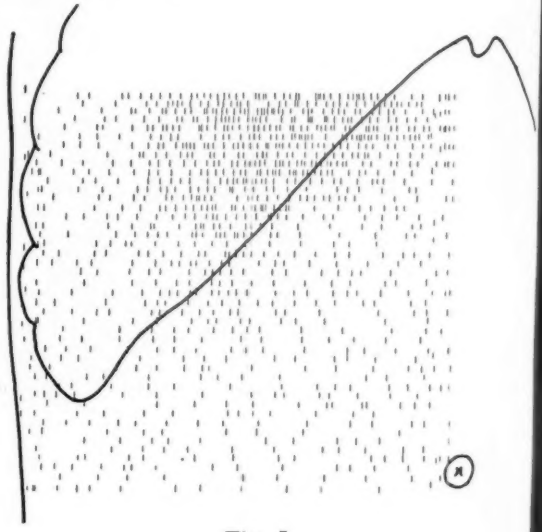

Fig. 5.

Fig. 4.—Cholescintigram of a patient with proved normal gall bladder function. Note the focus of increased radioactivity in the region of the gall bladder.

Fig. 5.—Cholescintigram of a patient who had been previously subjected to cholecystectomy. Note that some radioactivity is recorded over the liver area, as in Fig. 4, but that no focus of activity is present in the region of the gall bladder.

quadrant which corresponded to the anatomic position and configuration of the gall bladder (see Fig. 4). The appearance and disappearance of this area of radioactivity followed the same pattern as that observed in the animal experiments.

The remaining four patients were selected because gall bladder function was absent in each. Two had been subjected to cholecystectomy, and repeated cholecystography in the other two had failed to permit visualization. Concentration of the radioactivity in the liver area appeared, as previously described, within fifteen minutes after administration of DIF; however, the cholescintigram failed to demonstrate any evidence of concentration of radioactivity in the area of the gall bladder. Observations were continued for four hours after injection, and the absence of concentration in this area was confirmed (Fig. 5).

Thyroid uptakes were obtained routinely, and no significant uptake of the DIF was observed.

DISCUSSION

Intravenous cholecystography has long been recognized as the most reliable method of roentgenologic visualization of the gall bladder.[4] However, toxic side reactions are frequent, and the mode of administration is cumbersome. With the introduction of orally administered contrast substances, the intravenous technique was virtually abandoned.

Although oral cholecystography is adequate in the majority of cases, it has certain limitations.[2] Patients are not infrequently encountered in whom oral medication is either contraindicated or not feasible, for example, patients who are vomiting or who require gastric suction. Also, in the differential diagnosis of acute abdominal pain, the time delay required to perform oral cholecystography may, under certain circumstances, preclude its use.

Cholescintography may offer the clinician a nontoxic, intravenous procedure for visualization of the gall bladder. The amount of DIF required for performing cholescintography averages 0.3 Gm., which is less than 10 per cent of the amount of contrast medium used for intravenous cholecystography. It is for this reason that toxic side effects are absent. This technique demonstrates the presence or absence of gall bladder function even in instances in which only minimal function is present. However, the technique has not as yet been developed sufficiently to demonstrate biliary calculi.

Further clinical trials are in progress to establish the reliability of this technique as a routine clinical procedure.

Acknowledgments.—We wish to express our gratitude to Dr. R. L. Libby of the radioisotope unit, whose cooperation and assistance greatly aided in the development of this technique, and to Mr. Manuel Tubis of the unit, who prepared the DIF used in this study.

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THE SURGICAL CORRECTION OF PANNICULUS ADIPOSUS ABDOMINIS

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INTRODUCTION

REPORTS in the literature of the operative removal of a large dependent fatty abdominal apron are sufficiently sparse to justify the addition of two more cases. The condition with indications for surgical removal is common enough that any helpful details in the technique of management should be made readily available to those confronted with such problems. If more reports of such cases are added to the literature, it is probable that knowledge concerning the pathogenesis of this condition will accrue. These are the purposes of this report.

It is not known why some obese persons develop a large dependent panniculus, and why others do not. Bickham[1] suggested that the condition may be etiologically related to multiparity in obese women.

The primary indication for surgical attack on panniculus adiposus abdominis is the restriction on physical activity. Cosmetic considerations constitute a secondary indication, the validity of which should be evaluated on the basis of the individual patient. Bickham[1] stated, "As the condition seriously and mechanically handicaps the patient—interfering with bodily care, with sexual intercourse, with dress, causing intertrigo, and the like—the removal of the fatty mass is often indicated—and has been frequently successfully performed."

Gould and Pyle[2] illustrated a case of a patient with a large abdominal apron of fat dependent to the knees.

The following quotation from Bickham[1] reflects knowledge of the need for radical excision of the panniculus abdominis. "And Kelly removed one such abdominal apron (complicated in his case, however, by an umbilical hernia) in which the patient weighed 464 pounds . . . In Kelly's case a piece of tissue measuring, vertically, 19 inches and, transversely, 36 inches, was removed. The wound healed perfectly, and the patient was reported in excellent health eight months afterward . . . In some cases the ellipse has begun within three inches of one side of the spine, and extended to the corresponding site upon the opposite side—thus entirely circumventing the patient with the exception of some six or eight inches."

Short[3] reported a case of extreme obesity in a 32-year-old white woman whose weight was reduced from 395.5 pounds to 156.5 pounds in twenty

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months by diet restriction and thyroid extract. When she weighed 177.5 pounds, surgery was performed for the removal of an abdominal apron. The specimen weighed five and one-half pounds, and measured twenty-four and one-quarter inches in length and twelve and one-quarter inches in width.

A. *B.*

Fig. 1 (Case 1).—Preoperative photographs taken on June 5, 1951, showing the giant panniculus and umbilical hernia. *A*, Anterior view, and *B*, oblique view showing one of the smaller accessory aprons.

Smith[4] performed a panniculectomy on a 41-year-old Negro woman who weighed 321 pounds and was seventy-one inches tall. The panniculus developed over a period of five years and hung almost to the knees. It interfered with her usual activities and caused severe intertrigo. Each limb of the elliptical incision was thirty inches long. The excised mass weighed fifty-seven pounds, and it measured twenty-seven inches transversely, twenty-three inches vertically, and twenty inches in depth. Enlarged veins were encountered in the subcutaneous fat and Smith admonishes that, therefore, meticulous hemostasis is of utmost importance. The wound drained for three weeks from fat necrosis, but otherwise healed well.

Jackson and Steeper[5] introduced the idea of suspending the large panniculus to an overhead frame as a means of facilitating the operation. The patient was a 45-year-old white man who gave a six-year history of develop-

ment of the apron, beginning when he was bedridden with a compound leg fracture. During this time he reached a maximum weight of 700 pounds. He weighed 450 pounds at the time of the operation. The apron measured three and one-half feet across the base and one and one-half feet across the distal end, and hung to within a few inches of the ankles. This huge apron caused marked restriction of activity and was ulcerated at its distal end. The specimen weighed fifty-three pounds after drainage of blood and serum. Large veins were encountered at the time of surgery, and postoperatively the patient went into shock because of the formation of a large hematoma in the wound. The wound was 95 per cent healed in six weeks.

We wish to add our experience with this interesting disease in the form of two case reports.

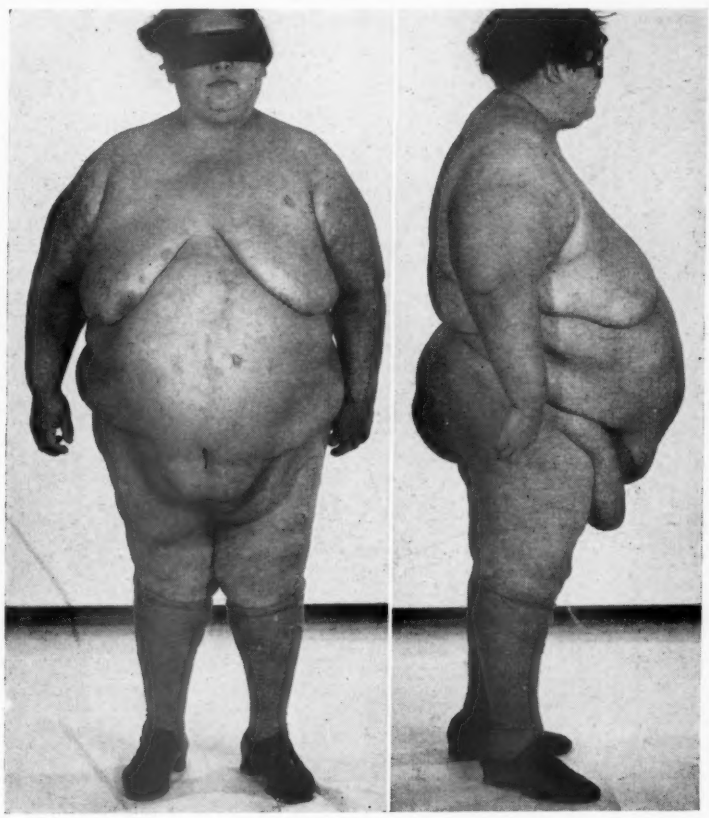
Fig. 2 (Case 1).—Photograph taken at the time of surgery showing both the overhead suspension of the panniculus and the presence of the accessory aprons.

CASE REPORTS

CASE 1 (No. 146099).—M. M., a 41-year-old Indian woman, was first admitted to the medical service of the King County Hospital on April 23, 1950, because of bronchopneumonia. She had been bedridden for the preceding three years because of the presence of a tremendous unmanageable panniculus abdominis which hung down almost to the ankles. The skin of the most dependent portion of the apron was indurated and ulcerated. She had weighed at least 300 pounds for the preceding twenty years. She had had ten pregnancies, only one of which went to term. The patient was cured of pneumonia without difficulty, and she was advised to have a panniculectomy in one month. She refused surgery, and was not seen again until June 3, 1951, when she was again admitted to the medical service because of abdominal pain, fever, and urgency and frequency of urination. The signs and symptoms rapidly abated spontaneously, and no conclusion was reached regarding the etiology.

She was persuaded to submit to resection of the large abdominal apron on this admission. On June 4, 1951, her weight was recorded as being between 295 and 300 pounds. She was sixty-one inches tall. The umbilicus was twenty-nine inches above the floor; the greatest width of the panniculus was twenty-two inches; the tip of the apron was only ten inches from the floor; the tip of the xiphoid process was forty inches above the inferior extremity of the panniculus; and the circumference of the apron seven inches below the umbilicus was thirty-seven inches (Fig. 1, *A* and *B*).

On June 15, 1951, in preparation for operation, two Crutchfield tongs were placed into the distal extremity of the apron. Then, by means of a rope and pulley, the giant apron was hoisted above the supine patient (Fig. 2). The skin was then prepared with soap and water, ether, and tincture of Zephiran. A transversely oriented elliptical incision measuring seventy-one inches in circumference was then made around the base of the panniculus. The subcutaneous fat was incised down to the fascia of the external oblique and rectus muscles. Many large blood vessels were encountered during the course of the



A. *B.*

Fig. 3 (Case 1).—Postoperative photographs taken on Dec. 2, 1952, seventeen and one-half months after surgery. *A*, Anterior view, and *B*, lateral view, both showing accessory aprons.

dissection. Some of the veins approached 1 cm. in diameter. Meticulous care was employed in securing hemostasis. A moderately large umbilical hernia was present; this was repaired by vertical imbrication, using nonabsorbable sutures. A large, smooth, lower abdominal cystic mass was noted. The nature of this mass was not discovered at the time of surgery because it was thought unwise to add the trauma of intra-abdominal manipulation to the large operation of panniculectomy. The extreme obesity precluded the preoperative identification of the mass. Subsequent abdominal exploration was urged, but

the patient refused this. No additional buried sutures were used to close the skin and subcutaneous tissue. Instead, these were approximated with No. 30 stainless steel wire mattress sutures tied over two segments of rubber tubing on each side of the incision. A soft rubber drain was placed in each extremity of the incision. The closed incision measured thirty-three inches in length. The specimen weighed forty-three and one-half pounds after the blood and serum were drained. Healing was slow, and some serum and necrotic fat drained from the drain sites until complete epithelization occurred six weeks after operation. The patient was discharged from the hospital on the nineteenth postoperative day. Eight months after operation she weighed 281 pounds and was able to carry on normal activity. Seventeen and one-half months postoperatively she weighed over 300 pounds, and the accessory aprons appeared larger than before (Fig. 3, *A* and *B*). She had made no effort to restrict her diet.

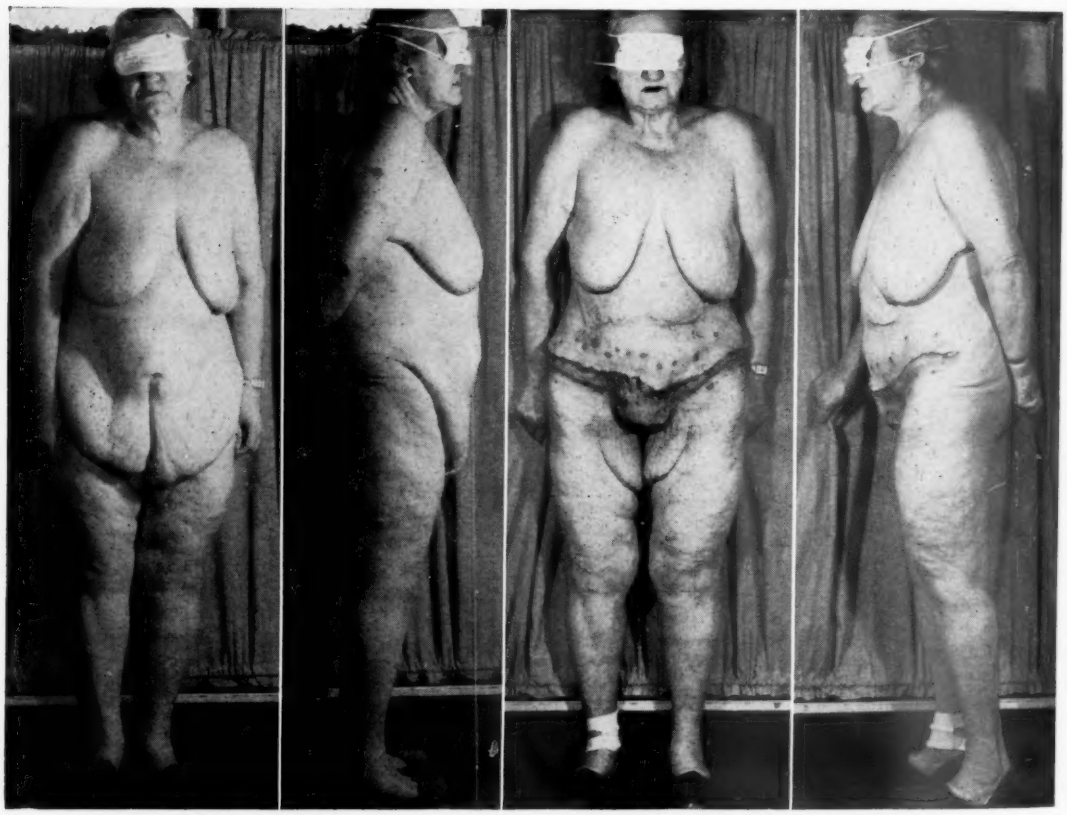


Fig. 4, *A*. Fig. 4, *B*. Fig. 5, *A*. Fig. 5, *B*.

Fig. 4 (Case 2).—Preoperative photographs taken on March 24, 1952, showing the dependent panniculus. *A*, Anterior view, and *B*, lateral view.

Fig. 5 (Case 2).—Postoperative photographs taken on April 11, 1952, eight days after surgery. *A*, Anterior view showing the accessory aprons, and *B*, lateral view.

CASE 2 (No. 122240).—H. B., a 52-year-old white woman, had been known to have had diabetes for twelve years. She had had only one pregnancy known to us. She was first seen by us on March 15, 1952, with a moderately large abdominal panniculus of unknown duration. She weighed 188 pounds and was sixty-two inches tall. The apron hung down almost to the mid-portion of the thighs (Fig. 4, *A* and *B*). She had moderately severe intertrigo, probably made worse by the occasional spillage of sugar in the urine. On April 3, 1952, she was taken to surgery. The overhead suspension technique, as employed in Case 1, was used in this

case. An umbilical hernia 5 cm. in diameter was present. The excision, repair of the umbilical hernia, and closure were performed as in Case 1. Again many large-caliber veins were encountered. The resected specimen, drained of blood and serum, weighed ten and one-quarter pounds. The length of the closed incision was twenty-three and one-half inches. The patient was discharged from the hospital on the eighth day after operation (Fig. 5, *A* and *B*). Subcutaneous serous fluid had to be aspirated on several occasions for the first six postoperative weeks, at the end of which time the operative area was well healed. The intertrigo healed, and she was able to carry on her activities with more comfort. Five months after operation she weighed 184 pounds. She was not heard from again until Sept. 22, 1952, at which time she was brought into the emergency room dead on arrival. No further information was available.

DISCUSSION

Several interesting features become apparent from the study of our cases as well as those of others. A fairly consistent finding is the presence of large veins and arteries in the subcutaneous fat. This is not surprising when one considers that there is a larger amount of tissue to be vascularized by the abdominal wall plexus than is normally the case. Air embolism is at least a theoretical hazard during surgery, although it has not been described. The main danger, however, is shock from loss of blood and, therefore, careful estimation of blood loss and volume-for-volume replacement are in order. Neither of our patients developed shock. One of us (H. N. H.) saw a patient die of shock following panniculectomy at a time (1928) when adequate blood transfusions were not regularly given.

Umbilical hernia was present in both of our cases and also in several cases collected from the literature. Whether or not there is an etiological relationship between umbilical hernia and the huge fatty apron is open to conjecture.

The technical maneuver of overhead suspension of the panniculus at the time of surgery is quite useful from the standpoints of facilitating operation and also of causing gravity drainage of part of the blood in the enlarged blood vessels back into the patient.

Healing of the wound is quite slow, as would be expected because of the excessive amount of fatty tissue and fat necrosis. Meticulous hemostasis is essential to avoid wound infection and to promote better healing.

Smaller accessory aprons of fat were noted in both of our cases arising from the medial aspect of the inguinal creases (Figs. 1, *B*, 2, 3, *A*, 3, *B*, and 5, *A*). We made no attempt to excise these accessory aprons, although from the standpoints of intertrigo and appearance this should be considered when they are present.

Pathologic examination of the specimen in Case 1 revealed ulceration, edema, and thickening of the skin in the most dependent portion. These changes comprise another indication for surgical removal of the panniculus. This was also noted in the case cited by Jackson and Steeper.[5]

SUMMARY AND CONCLUSIONS

1. Two surgically treated cases of panniculus adiposus abdominis are presented.

2. The indications for surgical removal are restriction of physical activity, ulceration, intertrigo, and cosmetic considerations.

3. The pathologic changes, including ulceration, edema, and oversized blood vessels, are described.

4. Umbilical hernia and smaller accessory aprons are sometimes associated with the large panniculus.

5. Overhead suspension of the fatty mass affords greater technical facility of excision.

6. The results of indicated surgical treatment of panniculus adiposus abdominis are gratifying to both the patient and the surgeon.

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EXCRETION OF ANTIBIOTICS, DYES, AND RADIOACTIVE SUBSTANCES THROUGH EXTERNAL PANCREATIC FISTULA

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THE excretion of various substances through the pancreas in human beings has been extensively studied by two methods. Indirectly, duodenal contents have been aspirated by various ingenious devices. Directly, secretions have been collected through an external pancreatic fistula. The former method is complicated by possible or actual admixture of stomach secretions, succus entericus, and bile with the pancreatic secretions. It is therefore more useful in a study of the pancreatic enzymes, as compared to a study of electrolytes or substances which might also be secreted or excreted in the other juices. In the latter method, it must always be remembered that a pathologic state is present, albeit one which releases physiologic tensions in a portion of the pancreas which cannot rid itself of external secretions through the normal anatomic passages. Excretions of penicillin, streptomycin, Aureomycin, chloromycetin, terramycin, radioactive diiodofluorescein, radioactive iodinated human serum albumen, phenolsulfonphthalein, and Congo red through an external pancreatic fistula were studied.

CASE REPORT

A 43-year-old white man, a laborer, was admitted on April 6, 1951, with a diagnosis of recurrent pancreatitis. Serum amylase rose to 240 units (normal up to 40) and serum lipase to 200 units (normal up to 120). On June 11, 1951, a pancreatic cyst presenting between the stomach, spleen, and splenic flexure of the colon was marsupialized. Two liters of a green viscid fluid was evacuated. Analysis of this fluid revealed 181 units of amylase and 436 units of lipase. The patient's postoperative course was uneventful, except for the persistence of an opening in the center of the scar through which there was continuous discharge of an opalescent fluid. It produced a severe skin excoriation, which was controlled by inserting a small polyethylene tube into the fistulous tract to prevent secretions from coming in contact with the skin. The secretion was collected in a bottle fastened to the abdomen by means of adhesive tape. Sinograms, using Lipiodol, revealed a blind pocket internally, with no evidence of connection between the tract and any pancreatic ducts which may have been normally draining into the duodenum. (See Fig. 1.)

The fluid was clear, colorless, and slightly opalescent with an average pH of 8.3 (varied from 7.4 to 9.0). Amylase content averaged 1,350 units, lipase content 435 units. The average amount of secretion was 58 c.c. per twenty-four hours (varied from 12 to 72 c.c.). Secretin increased, while atropine, Banthine, and gastric suction decreased the amount of fluid. Tests of this fluid were made as described herewith.

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The patient's gastrointestinal function was excellent with no evidence of pancreatic deficiency. The secretion persisted and on April 28, 1952, the abdomen was re-explored. The fistulous tract joined the tail of the pancreas about 3 cm. from its tip. The tail of the pancreas (4 cm. in length) was resected with the fistulous tract en bloc. The pathologic diagnosis was reported as a sinus tract with surrounding fatty tissue attached to a portion of pancreatic tissue. (See Fig. 2.) Histologically, interstitial fibrosis of the pancreas and granulation tissue, fibrosis and fat necrosis of the mesentery, and fibrosis of the skin were reported. The patient had an uneventful recovery, except for the persistence of pain in the left lumbar region for which no explanation could be found. The pain disappeared spontaneously one month postoperatively. The patient has felt well with no signs or symptoms of pancreatic deficiency.

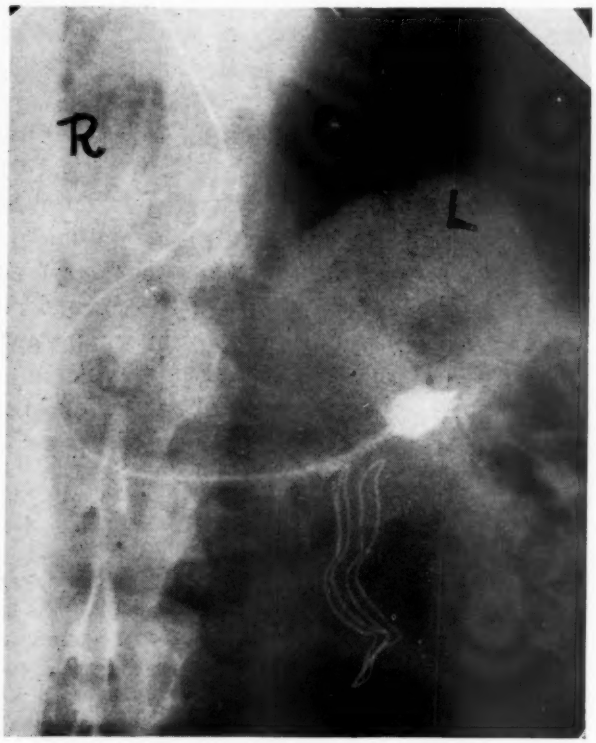

Fig. 1.—Sinogram of tract and pseudocyst pocket in tail of pancreas.

METHOD OF STUDY

Antibiotics were administered in the most commonly used forms and dosages except for penicillin as noted later in this article. Samples were collected in the morning twenty-four and forty-eight hours after the first dose was given. Since bacterial contamination was early noted as a complication of this procedure, a sufficient amount (10 c.c. or more) was collected, and passed through a Seitz filter. Tests were performed on this filtrate and on a blood specimen drawn at the end of the collection period. Known concentrations of the antibiotic tested were compared to the test serum or secretion and the amount of inhibition of growth of bacterial colonies was compared.

Penicillin (penicillin G potassium-crystalline), 300,000 U. dissolved in 3 c.c. of saline solution, was given intramuscularly every four hours. *Staphylococcus*

aureus was used as the test organism in broth culture. These cultures were incubated overnight.

Streptomycin (calcium chloride complex), 0.5 Gm. dissolved in 1 c.c. of saline solution, was given intramuscularly every six hours. *Bacillus subtilis* was used as the test organism on agar plates. These cultures were incubated overnight.

Aureomycin (as the hydrochloride), 250 mg. capsules, was given orally every six hours. *Bacillus cereus* was used as the test organism in broth culture. Incubation was conducted for four hours because of the known instability of Aureomycin over long periods of time.

Chloromycetin (chloramphenicol), 250 mg. capsules, was given orally every six hours. *Shigella sonnei* was used as the test organism in broth culture. These cultures were incubated overnight.

Terramycin (as the hydrochloride), 250 mg. capsules, was given orally every six hours. *Staphylococcus aureus* was used as the test organism in broth culture. These cultures were incubated overnight.

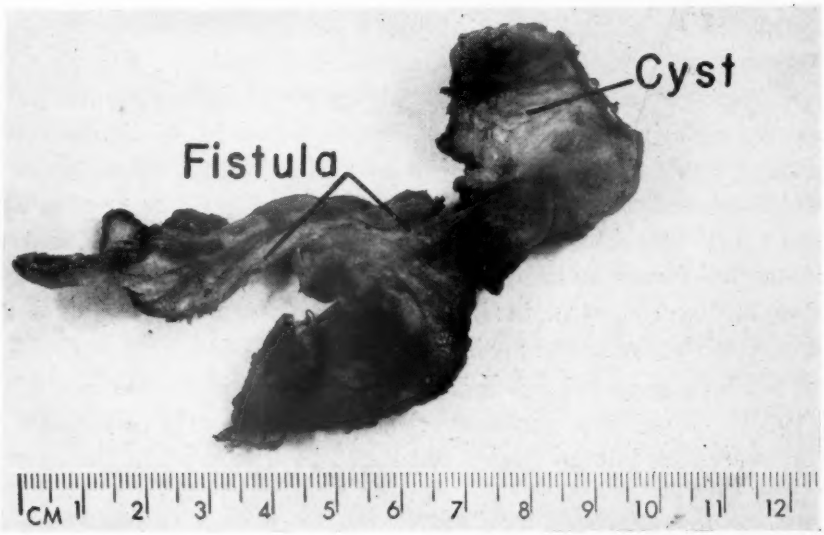

Fig. 2.—Specimen of fistulous tract and opened pseudocyst in tail of pancreas.

Dyes used were:

Phenolsulfonphthalein, 6 mg. of the monosodium salt in 1 c.c., administered intravenously. Samples of pancreatic fluid were collected at fifteen-minute intervals for one hour.

Congo red, administered as 10 c.c. of an equivalent to 0.6 per cent disodium diphenyldiazo-bis-alphanaphthylaminesulfonate solution, given intravenously. Samples were collected at fifteen-minute intervals for a period of one hour.

Radioactive substances used were:

Iodinated human serum albumen, 215 μc in one dose orally. Specimens of secretions, blood, and urine were collected at regular intervals for twenty-

four hours. Thyroid radioactivity measured with a Geiger counter, was noted at regular intervals for twenty-four hours.

Diiodofluorescein, 195 μc administered in one dose orally. Specimens of secretion, plasma, and urine were collected at regular intervals for twenty-four hours.

RESULTS OF TESTS

Antibiotics.—

Results are tabulated in Table I.

TABLE I

ANTIBIOTIC	SERUM CONCENTRATION		SECRETION CONCENTRATION (UNITS PER CUBIC CENTIMETER)	
	24 HOURS	48 HOURS	24 HOURS	48 HOURS
Penicillin	10	5	0	0
Streptomycin	11*	11*	0	4*
Aureomycin	3.2*	1.5*	0	0
Terramycin	1.5*	1.5*	0	0
Chloromycetin	0	0	0	0

*In μg per c.c.

Dyes.—

Congo red: On one occasion, dye appeared in the pancreatic juice. This was measured colorimetrically against known dilutions of Congo red in pancreatic juice. Each specimen was diluted 1:40 with normal saline solution to give sufficient quantity for colorimetric analysis. Klett-Summerson was standardized on a 1:10,000 solution of Congo red. A 1:2,220 concentration of Congo red solution was found in the pancreatic excretion collected in the first fifteen minutes; a 1:930 concentration in the second fifteen minutes; and a 1:1,150 concentration in the final one-half hour of collection.

This test was repeated on two subsequent occasions. On one of these occasions, 100 U. of secretin was also injected intravenously to increase the total amount of secretion, but no Congo red could be discerned in the external pancreatic secretion.

Phenolsulfonphthalein:

None was discernible in the pancreatic secretion.

Radioactive substances:

a. Iodinated human serum albumen: Clearance of this substance, as measured by the radioactivity of the secretion, proceeded at a regularly increasing rate up to twenty-four hours. At the end of the test period it was being cleared at the rate of .005 per cent of the injected dose per hour. Urine clearance and disappearance of iodinated human serum albumen from the blood were normal as compared to the same factors in other patients in whom this substance had been used.

b. Diiodofluorescein: Clearance of this substance was analogous to that of iodinated human serum albumen, as noted previously.

DISCUSSION

Antibiotics.—Despite the more than adequate blood levels of penicillin, none could be demonstrated in the pancreatic secretion. Good blood concentrations were obtained for Aureomycin and terramycin, with none apparent in the pancreatic secretion. Chloromycetin was absent in both the blood and pancreatic secretion tests. Streptomycin, on the other hand, was present in good concentration in the blood, and in fair concentration in the pancreatic juice.

Therefore, it is apparent that streptomycin administration would be a valuable adjunct to the established methods of treatment for pancreatic disorders requiring bacterial control. Inasmuch as Aureomycin and terramycin were not excreted, their effect on pancreatic diseases of a bacterial nature would be dubious. Chloromycetin showed little effect on the test organism used, even in the control dilutions, and consequently no deductions can be made from this test.

The role of penicillin in the treatment of pancreatic disorders is more difficult to evaluate. According to these tests penicillin was not excreted in the pancreatic secretions or was inactivated by a penicillinase. In a similar case, Howard and co-workers[7] reported "high concentrations of penicillin detected" after an injection of 300,000 U. of procaine penicillin G followed fifteen hours later by an injection of 400,000 U. of crystalline penicillin. In a personal communication, Howard stated that his results have been confirmed in several other patients.

It must be kept in mind that there may not be complete correlation between the concentrations of antibiotics in pancreatic tisues and their appearance in the external secretion of the pancreas.

Radioactive Substances.—The concentrations of iodinated human serum albumen and diidofluorescein obtained in the pancreatic secretion correspond to those expected to be present in any body fluid by simple diffusion. Therefore, no special activity of the pancreas to circulating albumen or fluorescein can be assumed. In the former substance (iodinated human serum albumen), studies of the chemical components in the pancreatic secretion revealed that most of the radioactivity was present in free iodine.

Dyes.—According to several previously published studies on animals,[8-10] Congo red is not excreted in pancreatic secretion. In our first attempt, Congo red was obtained in good concentration in the secretions obtained through the tube in the pancreatic fistula. These results could not be repeated on two subsequent attempts, even with secretin stimulation of pancreatic secretion. Detailed study of all factors of each test revealed no possible external or internal influence to account for the discrepancy between these tests. However, it was noted that on occasions blood would appear in the pancreatic secretion, probably because of irritation produced by the indwelling tube on the granulation tissue at the base of the fistula. Although no blood was found in the pancreatic secretion containing Congo red, it is likely that Congo red was carried to the effluent of the tube via serum which was extruded from the granulation tissue.

The absence of phenolsulfonphthalein in the pancreatic secretion confirms findings of previous experiments in animals.

COMMENT

The characteristics of pancreatic fluid, as well as the effect of various foods and drugs on the amount and the type of secretion, have been well described by many authors.[1-6] Our findings have in general approximated those previously reported and, therefore, are not being described here in detail.

Of special interest is the result of attempts to decrease the function of the pancreas as measured by the amount of secretion obtained from the fistula. By the use of gastric suction to decrease humoral stimulation of the pancreas and Banthine to decrease neural stimulation, the amount of secretion obtained through the fistula decreased from an average daily amount of 58 to 20 cubic centimeters. The amylase concentration of the fluid obtained rose to 3,100 units per cubic centimeter. The lipase concentration rose to 2,015 units per cubic centimeter. The fluid appeared more viscid and opalescent, and became slightly cloudy. After forty-eight hours of suction and Banthine, the patient complained of epigastric distress and nausea, with pain over the area of the tail of the pancreas, radiating to the left of the second lumbar vertebra. He described this pain as being similar to that of attacks prior to insertion of the tube into the fistula, at which times elevated serum amylase and lipase were found. This attack required several injections of Demerol and atropine for relief. The tube in the fistula was removed, cleansed of inspissated material, and replaced. The attack thus subsided after twenty-four hours, with a total twenty-four-hour secretion of 12 cubic centimeters. The secretion of the next twenty-four-hour period, during which the patient was feeling well, was 44 c.c. and three days after the attack the secretion rose to average daily volume.

This occurrence raises the question of the advisability of "drying up" pancreatic secretion in pancreatic disorders, especially acute pancreatitis or acute exacerbations of chronic relapsing pancreatitis. The episode described here would indicate that a thicker, more concentrated secretion may be followed by two unfavorable possibilities. (1) The increased viscosity may lead to plugging of a duct or channel already narrowed by edema, inflammation, or scar tissue. (2) The increased concentration of enzymes may lead to increased digestion of pancreatic and peripancreatic tissue if there is an actual leak of pancreatic juices from their normal habitat in the acini and ducts.

These possibilities are mentioned as questions rather than conclusions. They serve to indicate the urgent need of further investigation of the pathologic physiology of pancreatic disorders and the actual effect of the various recommended methods of treatment.

CONCLUSIONS

1. Of the available antibiotics, streptomycin was excreted in secretion obtained through a pancreatic fistula. Penicillin, Aureomycin, and terramycin were not found in pancreatic excretion. No conclusion can be drawn on chloromycetin excretion.

2. Excretion of radioactive iodinated human serum albumen and radioactive diiodofluorescein revealed no special activity of the pancreas to either

substance. Amounts obtained in the pancreatic secretion closely correspond to the amounts expected in tissue fluids.

3. Neither Congo red nor phenolsulfonphthalein were excreted in the pancreatic secretion.

SUMMARY

A case of external pancreatic fistula followed marsupialization of a pancreatic cyst is presented. The excretion of certain antibiotics, radioactive substances, and dyes through an external pancreatic fistula was studied. Tests were conducted on volume and type of secretion through this fistula.

The advisability of drying up pancreatic secretion in pancreatic disorders is raised as an incentive to further investigation.

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AN EVALUATION OF ESOPHAGITIS IN DOGS FOLLOWING THE HELLER AND GRÖNDAHL OPERATIONS WITH AND WITHOUT VAGOTOMY

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THE correct surgical procedure for cardiospasm remains a controversial subject. The operation of choice in this country has been esophagogastrostomy with cardiotomy (Gröndahl) for some time. This procedure enjoyed apparent success in the hands of some surgeons until more recently when a generalized dissatisfaction has been voiced by many.[1, 2] This procedure undoubtedly alleviates the symptoms associated with cardiospasm; however, peptic esophagitis of varying degree is a most frequent sequela. The symptoms of esophagitis may be considerably more disabling than those of cardiospasm itself.

The Heller operation (extramucous esophagocardiomyotomy) has enjoyed a measure of success in England and on the continent, although performed infrequently in this country.[3, 4] Recently, it has been suggested that the Heller operation be performed for ordinary cases of cardiospasm and an extensive esophagogastrectomy be utilized for long-standing cases.[5] In view of the effects of vagotomy in reducing gastric secretion, some are tempted to utilize vagotomy to combat esophagitis following esophagogastrostomy.

This study was initiated in order (1) to evaluate experimentally the Heller and the Gröndahl operations, and (2) to study the effects of supplemental vagotomy.

EXPERIMENTAL CONDITIONS

Operative Procedure.—Thirty adult mongrel dogs were operated upon under Nembutal endotracheal anesthesia, utilizing aseptic conditions. Through a routine abdominal or thoracic incision, a classical Heller operation or a Gröndahl esophagogastrostomy was carried out. In addition, some animals in both groups were subjected to simultaneous bilateral vagotomy. In the performance of the Heller operation, the seromuscular layer was incised down to the submucosa. However, the craniocaudal length of the incision varied somewhat. In one group the incision transected the esophagogastric junction and extended 1 inch above and below it. Therefore, references made to the "short Heller" operation will refer to this group. A longer incision was made in other animals extending 2 inches above and below the presumed esophagogastric junction. This group will be referred to as the "long Heller" operation (Fig. 1*A* and Fig. 1*B*).

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METHODS OF STUDY

The operated animals were divided into four series as follows:

Group I (six dogs: three short Heller, three Gröndahl).—Postoperatively these animals received daily histamine-in-beeswax parenterally until death or sacrifice.

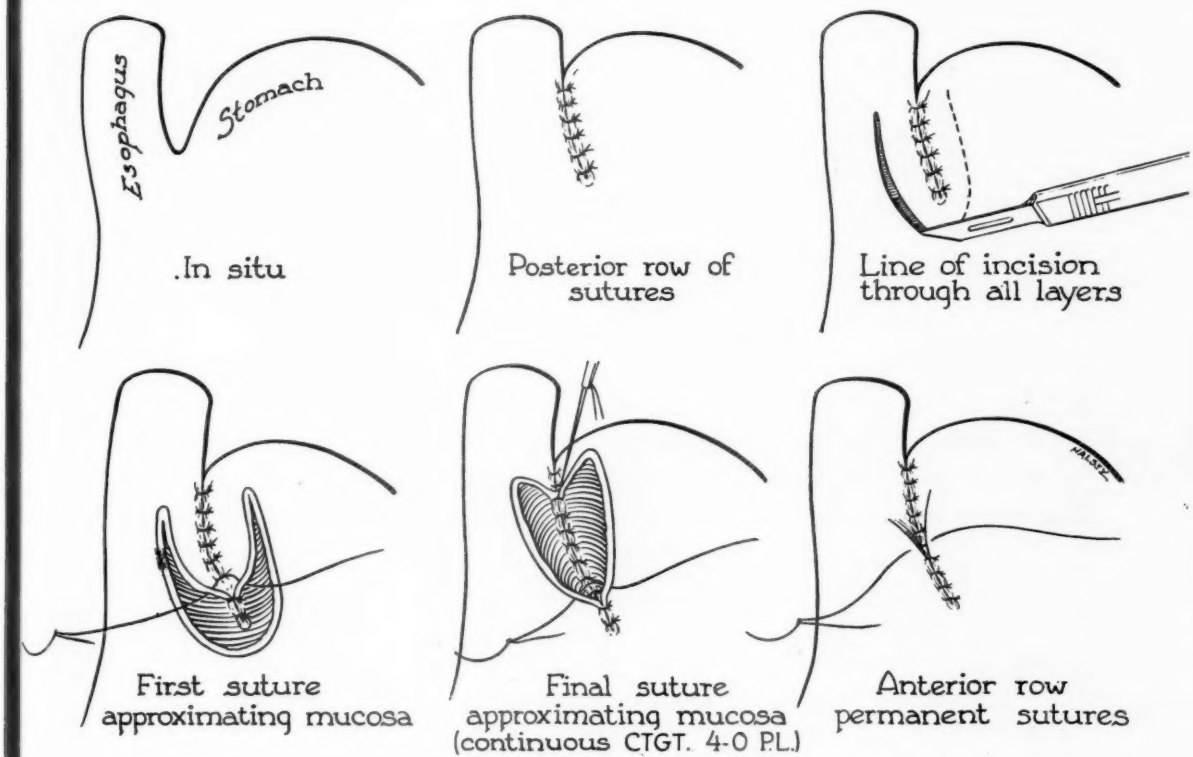

Fig. 1A.—Diagram illustrating the Gröndahl operation (esophagocardioplasty).

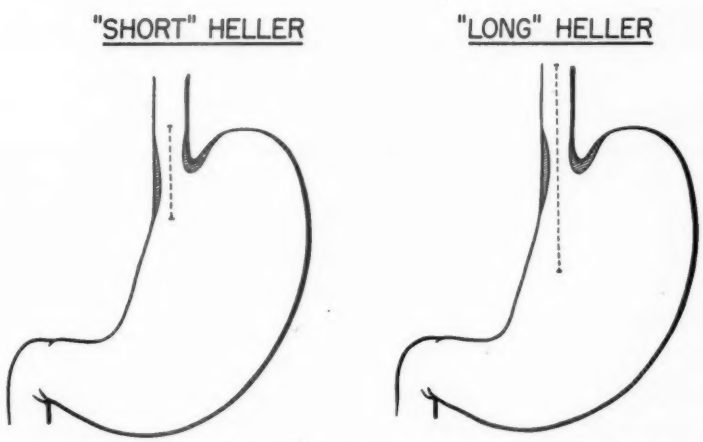

Fig. 1B.—Diagram indicating the length of incision for the short Heller and long Heller operations.

Group II (six dogs).—This group was identical in all respects to Group I with the single exception that in addition all animals were vagotomized.

Group III (twelve dogs: six short Heller, six Gröndahl).—In each subgroup one-half were vagotomized, and in the remaining one-half the vagi were intact. No histamine was administered. These animals were studied fluoroscopically following barium instillation in order to appraise gastroesophageal reflux.

Group IV (six dogs).—All were subjected to a long Heller operation. In addition, three had vagotomies, and three had vagi intact. Histamine-in-beeswax was administered daily for two weeks prior to sacrifice.

The histamine-in-beeswax was prepared in the usual fashion.[6] Thirty milligrams of histamine base was administered daily.

All surviving animals were sacrificed on the forty-second postoperative day. At autopsy the entire esophagus was removed. Tissue for microscopy was routinely taken from the esophagogastric junction and 10 cm. proximal.

RESULTS

A. *Specific Considerations.*—

1. *Gröndahl versus short Heller procedure* (Table I): Animals subjected to the esophagogastrostomy demonstrated greater esophageal sequelae than those having the short Heller operation. It is noted that all three perforations of the

TABLE I

SHORT HELLER*					GRÖNDAHL				
DOG NUMBER	NO PATHOLOGY	INFLAMMATION	ULCERATION	PERFORATION	DOG NUMBER	NO PATHOLOGY	INFLAMMATION	ULCERATION	PERFORATION
				A. Histamine Without Vagotomy					
E–50	+				E–52	+			
E–51	+				E–53		+	+	+
E–54	+				E–55		+	+	
				B. Histamine With Vagotomy					
E–61		+			E–56		+		
E–69	+				E–60		+	+	
E–70		+			E–72		+	+	+
				C. No Histamine					
				Without Vagotomy					
E–58	+				E–79		+		
E–73	+				E–59	+			
E–76		+			E–68	+			
				With Vagotomy					
E–75		+			E–67		+	+	
E–77		+			E–78		+		
E–80		+			E–74		+		

*Incision extended one inch above and one inch below (total 2 inches) esophagogastric junction.

esophagus occurred with Gröndahl-type procedures. In addition, a greater incidence of ulceration and esophagitis occurred in this group of animals. This observation is constant irrespective of the addition of vagotomy and/or the administration of histamine. With the addition of either or both of these

variables the pathology in both groups is enhanced. However, those animals with the Gröndahl esophagogastrostomy are affected more severely.

2. *Vagotomy versus nonvagotomy* (Tables I and II): Interruption of the vagi demonstrated a consistent aggravation of esophageal structure regardless of the primary operative procedure. Two of the three perforations occurred in vagotomized animals. In all series, there was an increased incidence of ulcerations and esophagitis in vagotomized animals.

3. *Effect of histamine* (Table I, *C*): This series of twelve animals was not given histamine. They were sacrificed in a corresponding time interval, i.e., forty-two days after recovery from surgery. There were no spontaneous deaths due to esophageal complications. As might be expected, without histamine stimulation there was lesser pathologic involvement of the esophagus. Again, an increased incidence of esophageal complications in the vagotomized animals was apparent.

4. *Long Heller series* (Table II): In this series the gastroesophageal muscular coats were stripped for a distance of 4 inches across the cardioesophageal junction. It is readily demonstrated in comparing Table II with Table I, *A* and *B* that the increased length of the muscular incision fosters greater esophageal pathology. This suggests that more extensive division of the "sphincter" or the interlacing myenteric neurogenic mechanism is necessary for complete paralysis

TABLE II. LONG HELLER SERIES* IN WHICH HISTAMINE WAS USED

WITHOUT VAGOTOMY					WITH VAGOTOMY				
DOG NUMBER	NO PATHOLOGY	INFLAMMATION	ULCERATION	PERFORATION	DOG NUMBER	NO PATHOLOGY	INFLAMMATION	ULCERATION	PERFORATION
E–81		+	+		E–83		+	+	+
E–82		+	+		E–84		+	+	
E–86		+			E–85		+	+	

*Incision extended 2 inches above and 2 inches below (total 4 inches) esophagogastric junction.

of the gastroesophageal junction. It is also apparent that the esophageal sequelae following the long Heller procedure are comparable to those following the Gröndahl procedure.

B. *General Considerations.*—The existence of several variables in the four series of animals does not allow a breakdown into percentages which would be significant. However, it is apparent that the short Heller operation offers some additional protection against esophagitis and its complications which the esophagogastrostomy procedure does not offer. However, when the long Heller operation is performed, the incidence of esophageal pathology increases and is roughly comparable to the results obtained by the Gröndahl procedure. Furthermore, when bilateral vagotomy supplemented all procedures, the incidence and severity of esophageal disease increased. Histamine administrations likewise adversely affected the results. In spite of a short observation period, the overall results in both operative groups were poor as evidenced by the following data: Of the thirty animals in the study, twenty-one (70 per cent) exhibited

esophageal pathology. There were three (10 per cent) perforations, seven (23 per cent) ulcerations other than those occurring with perforations, and eleven (36 per cent) with "peptic" esophagitis exclusive of those cases with perforation and ulceration. All perforations occurred in animals receiving histamine. Of twelve animals not subjected to the additional stimulus of histamine, one (8.3 per cent) developed esophageal ulcers, and seven (58 per cent) exhibited esophagitis. The high incidence, in this entire series, of esophageal complications, suggests that under these experimental conditions there is little to choose between either operative procedure (Fig. 2).

Fig. 2.—Specimens exhibiting the characteristic pathology associated with various operative procedures. From left to right in pairs: short Heller with vagotomy plus histamine, E-69 no pathology, E-61 slight inflammation; Gröndahl operation with vagotomy plus histamine, E-56 esophagitis, E-60 esophagitis with ulceration; long Heller without vagotomy but with histamine, E-82 and E-81 both are involved with esophagitis and ulceration.

The arrow in the middle specimen indicates a well-demarcated esophageal ulcer. In the last two specimens linear ulcerations can be seen extending up the esophagus.

Fluoroscopic examination of the esophagus following barium instillation revealed that one-half of the animals exhibited some delay in esophageal emptying. There was no correlation of this finding with the type of surgical procedure. There was likewise no correlation between delayed esophageal emptying, or the lack of it, and the resultant pathology.

At autopsy, the animals dead of esophageal perforation demonstrated gross inflammatory apertures immediately proximal to the operative site (Fig. 3). Associated pathology extended up the entire esophagus, diminishing in severity toward the pharynx. Obvious stomach contents were found in the pleural

cavities. When ulceration was the prominent finding, it was especially apparent on the crests of the longitudinal folds of the esophagus. Frequently the mucosa of the crests was denuded upward beyond 10 cm. Esophagitis alone was manifest by cornification of the stratified squamous epithelium of the mucosa, hyperplasia of the mucosa, submucosal vascular congestion and hemorrhage, and increased submucosal cellular elements consisting of polymorphs, macrophages, and fibroblasts. Of course, these same changes also were observed when perforation and ulcers were predominant.

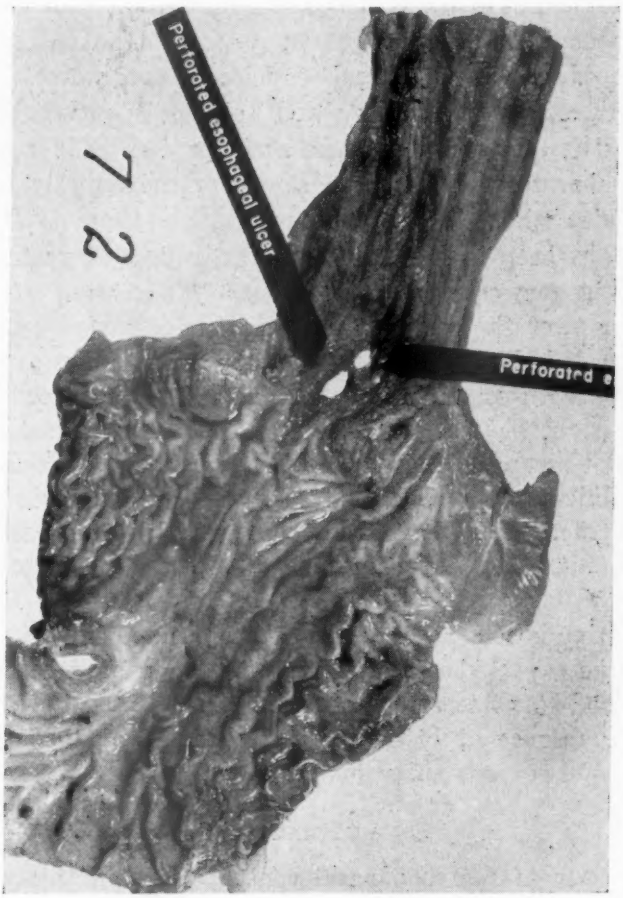

Fig. 3 (E-72).—Gröndahl operation with vagotomy plus histamine. The perforated ulcer is immediately proximal to the esophagogastric junction.

DISCUSSION

Cardiospasm cannot be produced experimentally with any regularity. Consequently, the evaluation experimentally of operations utilized clinically in its management cannot be expected to mirror completely the clinical result. In the absence of a definite cardiospastic area in the lower esophagus to attack surgically, it is sometimes difficult to determine the length that a craniocaudal incision (Heller) should be to mimic the clinical need. This resulted in the

utilization of short (2 inch) and long (4 inch) Heller operations. The results suggest that the long Heller operation allows easier regurgitation of the gastric contents into the esophagus.

By roughly comparing the length and size of gastrointestinal structures, the short Heller operation as performed in the dogs would appear to be adequate for the surgical management of cardiospasm clinically. The increased incidence and severity of esophageal pathology accompanying the long Heller operation suggest that the length of the incision may be important. In the absence of specific knowledge clinically of the mechanism of cardiospasm, the importance of quantitating the length of the craniocaudal incision is difficult to assess.

By the addition of bilateral vagotomy to either the Heller operations or the Gröndahl procedure the esophageal sequelae become worse. The advantage attending the reduced gastric acidity and volume is outweighed by the disadvantages of gastric atony, pylorospasm accompanied by increased esophageal reflux. In this laboratory, it has been shown experimentally in dogs that in upper gastrectomies where in the "sphincteric" mechanism at the esophagogastric junction has been excised with the restitution of gastrointestinal continuity by esophagogastrostomy, no "drainage" operation of any kind will either alleviate or alter the constant development of severe esophageal pathology.[7, 8] Therefore, it is highly unlikely that the combination of pyloroplasty or gastrojejunostomy with vagotomy in this study would exert any protective influence in the prevention of the esophageal lesions which developed in this study. This is not meant to imply that these results in dogs are transferable in toto to the clinical problem. The four-footed animal maintains the upper gastrointestinal tract in a horizontal plane. With the destruction of his sphincteric mechanism, regurgitation probably occurs more readily than in the upright human.

Histamine stimulation accentuated the development of the esophageal lesions as would be expected. Vagotomy per se would not be expected to protect against a blood-borne secretory stimulus.[9] However, the evidence is clear that even in the absence of histamine stimulation, vagotomy alone enhanced the development and severity of esophageal complications.

SUMMARY

1. A comparison of the esophageal complications in thirty dogs has been made following the Heller and Gröndahl procedures.

2. The incidence of esophageal pathology following both types of cardioplasties is considerable.

3. The Gröndahl procedure is accompanied by greater esophageal sequelae than the short Heller operation. However, these complications following the long Heller operation are about equal to those of esophagogastrostomy.

4. Vagotomy in conjunction with either procedure increases the incidence and severity of esophageal complications.

5. Histamine likewise accentuates these lesions regardless of the operative procedure, with or without vagotomy.

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Case Reports

SIMPLE PERFORATED ULCER OF THE COLON

Report of Two Cases

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Cruveilhier, in 1830, first described simple ulceration of the colon and, subsequently, several cases have been reported in the foreign literature. When Barron[1] summarized the subject in 1928, he was able to collect fifty cases from the library, in all but four of which[5, 8] the patients were of foreign descent. To this list he added three cases, and he then described the salient features of each case. Since then, the American and English literature has contained several more references to single ulcers of the large bowel.[2-4, 6, 7, 9-13] It is our desire to discuss this subject briefly and to present two additional cases.

The etiology of ulcerations in the stomach and duodenum is fully covered in any textbook of medicine, and the same etiological theories have been advanced regarding the initial lesions in other locations of the gastrointestinal tract; these theories are that their etiology may be neurogenic, circulatory, bacterial, toxic, digestive, or mechanical. Barron[1] quoted authors who believe that stasis seems to be a common denominator for a large percentage of the cases, with constipation as the chief complaint. He stated that fissuring may occur in the bowel, thus permitting secondary infection, hence an ulcer. Ischemia and venous stasis may be found with constipative distention, thereby promoting necrosis of the mucosa within a very short time. Because all of the ulcers seem to be chronic microscopically, fermentation and inflammation have frequently been considered as etiology. Barron further quoted authors who consider as etiological toxemia of the digestive tract with hemorrhagic necrosis due to infarcts, the presence of intestinal parasites, and disease of the vessels themselves, such as atheroma and endarteritis. Constipation, however, is so universal and widespread that it would seem likely that, if this were a frequent etiological factor, ulcer of the colon would be more common. Ulcers produced by foreign bodies would likewise seem to be more common if this were the cause. The exact origin of ulcer of the colon can probably be no better explained than the origin of the ulcer of the gastroduodenal mucosa and, indeed, the coexistence of the two is sufficiently common that it cannot be overlooked.

The diagnosis is outstanding in one simple fact, that is, it is not made preoperatively. Pain is a common complaint, and varies with the state of the disease. A simple shallow ulcer may give rise to very few symptoms or to

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vague indefinite abdominal pain which is frequently attributed to constipation. Obstruction in varying degrees may occur, adding to the signs and symptoms. Melena is occasionally present, and hemorrhage is rare; however, it does occur. Perforation makes the picture much more acute, with sudden severe sharp pain occurring at the point of perforation. Without treatment, generalized peritonitis arises within a short time. An inflammatory tumor may form and can be palpated. When this is present together with the acute inflammatory signs of perforation, a simple ulcer of the colon should be considered strongly. With the aid of barium studies of the colon, the diagnosis may possibly be made.

The entire picture is usually one of acute abdominal pain in which perforated appendix, acute cholecystitis, volvulus, strangulation, or intussusception should be considered. The location seems to be predominantly in the cecum (49.4 per cent),[2] and this common site makes the diagnosis virtually indistinguishable from that of an acute appendicitis. In fully 38.6 per cent of the cases, there was no diagnosis preoperatively and, in another 36.6 per cent, there was a diagnosis of acute appendix in one form or another. In a large majority of patients, perforation had already occurred, which led to the surgical treatment.

Grossly, the ulcers appear to be funnel-shaped and tend to perforate suddenly, eroding frequently into muscle. The edges seem hard and relatively chronic, but the base is very active, suggesting a lesion of slow onset, suddenly becoming acute. Cases reported in the literature include patients who range in age from 18 to 70 years, however, most ulcers reported occurred in patients between 40 and 50 years of age. Sex distribution is about 2 to 1 in favor of the male patients.

King[7] commented on the treatment of single ulcer of the colon with perforation as follows: "simple drainage, all died; oversewing with drainage, 9 patients, 7 survived; local excision with drainage, 5 patients, 4 survived; resection of the area with anastomosis, 11 patients, 10 survived; exteriorization and opening of the diseased area, 3 patients, 2 survived."

Moore[9] diagnosed his case grossly at surgery as neoplastic, and he resected the entire ascending colon. The patient made a satisfactory recovery.

CASE 1.—A 26-year-old white woman was admitted to the hospital on Feb. 5, 1952, on another service. Complaints were abdominal pain and anorexia of twenty-four hours' duration. During the evening and night before admission, she had been uncomfortable to the extent that she awakened her husband with groaning and grunting respirations. There was no history of change in bowel habits, jaundice, urinary findings, or previous episodes of abdominal pain. There was no change in the menstrual history. Movement was distressing to the patient.

On physical examination, the patient was said to "look sick" and was lying with knees drawn up, holding the abdomen. There was a Grade II systolic murmur over the mitral area. The abdomen was very tender throughout, with marked tenderness in the right lower quadrant and rebound tenderness in this area. Temperature was 100.6° F. orally, pulse 95, respiratory rate 18, and blood pressure 126/70. Laboratory findings were: urinalysis: acetone 3 plus, otherwise negative; blood count: hemoglobin 13.5 Gm., red blood count 4.4 million, white blood count 18,000; differential blood count: lymphocytes

6 per cent, monocytes 5 per cent, neutrophils 78 per cent, band cells 12 per cent, and eosinophils 1 per cent; amylase 66 units (normal 40 to 110); thymol turbidity 1 unit (normal 0 to 4 units).

The patient was operated upon the same day of admission with a preoperative diagnosis of acute appendicitis. The abdomen was explored through a McBurney incision,

Fig. 1.—Posterior perforation of the cecum may be seen as the lateral leaf of the mesentery is divided, exposing the posterior bowel wall.

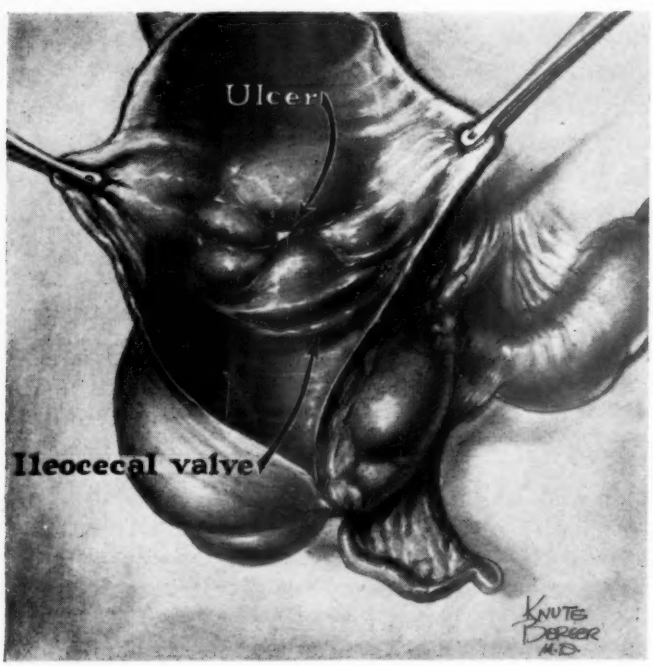

Fig. 2.—Perforated benign ulcer is seen in the removed specimen after opening the anterior cecal wall.

and the appendix was removed. The gall bladder contained "some stones of moderate size"; however, the organ was flaccid. The pelvis disclosed no abnormalities; there was no Meckel's diverticulum. A number of small mesenteric nodes, with one large soft node, were found in the mesentery superior to the cecum. The pathologist's diagnosis postoperatively was vermiform appendix. The patient developed peritonitis, and expired in forty-eight hours. Autopsy revealed a solitary ulcer of the transverse colon with perforation.

CASE 2.—A 31-year-old male sheet metal worker entered the hospital on June 6, 1952, with chief complaints of generalized abdominal tenderness, nausea, and vomiting, with constipation and localized tenderness in the right lower quadrant, all of about four days' duration. The family history and past history of the patient were essentially negative.

Physical examination revealed a well-developed, well-nourished man lying in bed, obviously in abdominal distress. Blood pressure was 136/70, pulse 100, respiration 20, temperature 100° F. orally. Laboratory reports on admission were as follows: urinalysis essentially negative; blood count: red blood count 4.6 million, hemoglobin 14.75 Gm., white blood count 11,400; differential blood count: lymphocytes 7 per cent, monocytes 10 per cent, neutrophils 78 per cent, band cells 5 per cent. After a clinical diagnosis of acute appendicitis, immediate surgery was elected. On exploration through a Rockey incision, a normal appendix was found. Further exploration revealed an inflammatory mass about 3 cm. above the ileocecal valve. A right colectomy with end-to-end ileocolostomy was performed by one of us (M. W. D.). The specimen revealed a chronic inflammatory ulcer of the ascending colon, perforated posteriorly and of undetermined etiology (Figs. 1 and 2). The patient made an uneventful postoperative recovery, and he was discharged on the sixth postoperative day.

SUMMARY

Simple nonmalignant ulcers of the colon may occur anywhere in the bowel, particularly in the region of the cecum, and although infrequently seen are sufficiently common that they should be recognized during the exploration of any acute abdominal emergency. The summary of the treatment as shown by others and as shown in Case 2 would indicate that immediate resection of the involved area and primary anastomosis is the treatment of choice.

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GASTRODUODENAL INTUSSUSCEPTION WITH MASSIVE HEMORRHAGE

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GASTRODUODENAL intussusception is a rare disease, and x-ray demonstration of the lesion is even rarer. In 1945, Hobbs and Cohen[1] collected from the medical literature and reviewed forty-one reports of this syndrome. Since that time, six more cases of gastroduodenal intussusception have been reported[2-6]; five of the intussuscepta originated from a benign tumor of the fundus of the stomach, that is, polyp, leiomyoma, lipoma, and adenoma. The sixth instance of intussusception was of spontaneous occurrence without preexisting abnormality in the stomach. Gastroduodenal intussusception occurs very rarely with malignant neoplasms of the stomach; in a series of 123 intussusceptions caused by malignant gastrointestinal tumors, only twice was gastroduodenal intussusception encountered,[7] whereas malignant gastric neoplasms make up over 50 per cent of all gastrointestinal malignancies. On the ward service at the New York Hospital from 1932 to 1950, there were approximately 1,700 gastric operations; yet, not one instance of gastroduodenal intussusception was encountered.

The patient constituting the basis for this report was admitted in October, 1950. He exhibited the classical symptoms of gastroduodenal intussusception, namely severe epigastric pain and gastrointestinal hemorrhage; in addition, the preoperative roentgenograms demonstrated enlargement of the duodenum, a filling defect of the duodenum, and distortion of the normal gastric contour.

CASE REPORT

I. D. (New York Hospital No. 580577), was a 62-year-old married man who was first admitted to the New York Hospital complaining of pain in the upper part of the abdomen and of weakness. He had been in perfect health until six days prior to admission to this hospital; at that time, after having ingested a large meal, he vomited some of the meal and felt extremely weak. He was admitted to the Terrace Heights Hospital in Long Island where the examining physician felt that the patient had suffered a coronary occlusion. However, electrocardiograms taken after the patient was admitted failed to substantiate this diagnosis. At that time, the patient was told he was "very anemic."

The abdominal pain decreased after the patient was in bed, and he was given a soft diet which he tolerated well. Two days after entering the Terrace Heights Hospital, he suddenly felt very weak, passed a large tarry stool, and went into shock. He received transfusions which elevated the blood pressure, but which failed to correct the profound anemia. Throughout the next four days, he continued to pass small tarry stools, and weakness continued. Gastrointestinal series taken at the Terrace Heights Hospital* revealed a most bizarre configuration of the stomach and duodenum which was interpreted as a "tumor of the second portion of the duodenum" (Fig. 1, *A* and *B*). Because the patient continued to bleed, he was transferred to the New York Hospital for further treatment.

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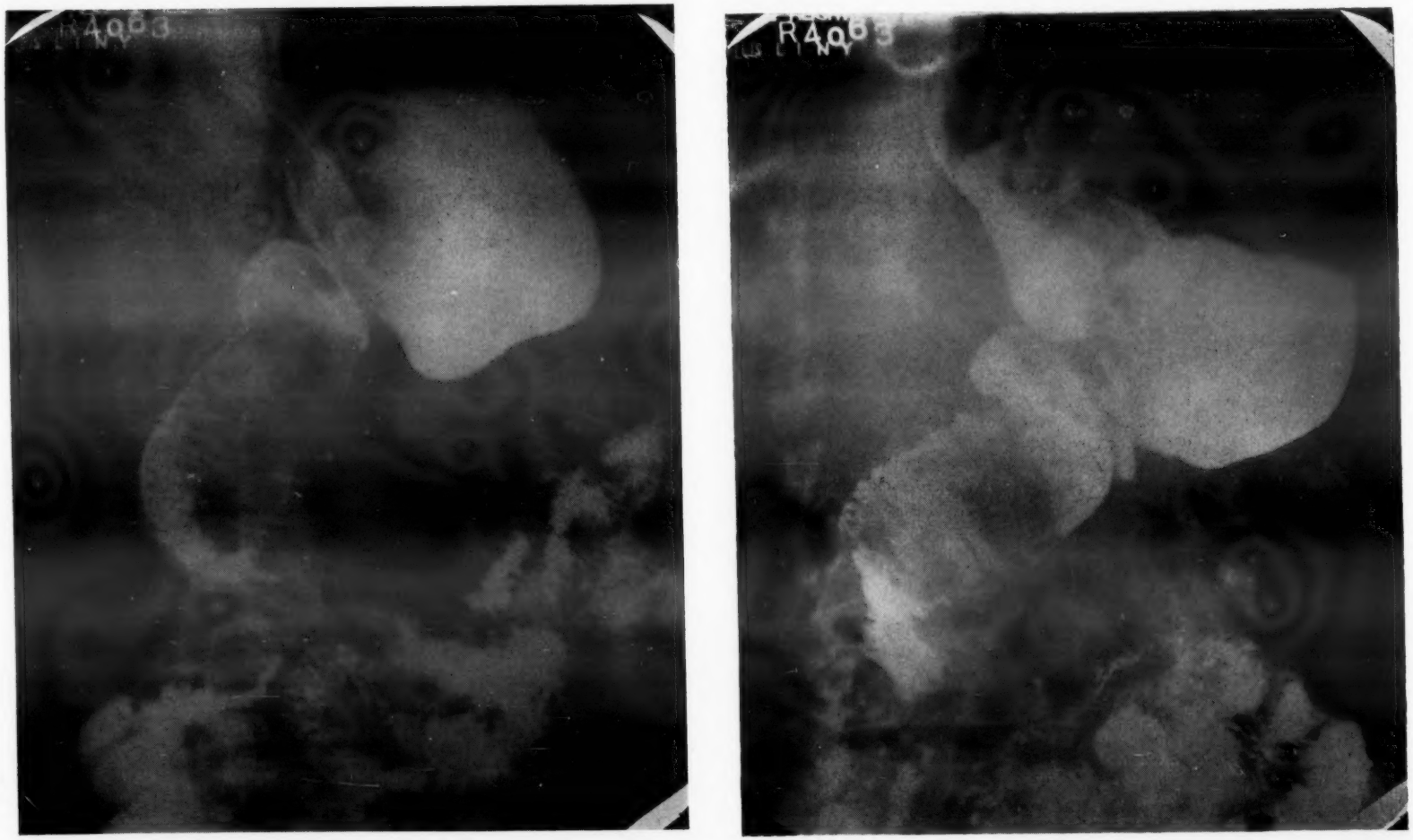
*We are indebted to Dr. A. N. Saperstein, Terrace Heights Hospital, Long Island, N. Y., for the use of his preoperative roentgenograms.



A. *B.*

Fig. 1 (I. D., New York Hospital No. 580577).—*A*, Preoperative roentgenograms demonstrating dilatation of duodenum and distortion of normal gastric shadow. *B*, Preoperative roentgenogram. This is very similar to *A* and, in addition, shows the wrinkling of gastric and duodenal wall, a classical picture in intussusception.

At no time in the past had the patient suffered from epigastric pain, "heartburn," tarry stools, or weight loss.

On entry to the New York Hospital, his temperature was 38.5° C., pulse 100 per minute, respirations 20 per minute, and blood pressure 170/80. The patient was quite pale, but in no great pain or distress. The only positive physical findings at that time were slight enlargement of the heart and a few crepitant râles at both bases of the lungs. The abdomen was flat, without distention, spasm, or tenderness. No masses could be palpated in the abdomen, and the liver and spleen were of normal size. Stool obtained during rectal examination was positive for blood.

Laboratory data on admission were as follows: urine: specific gravity 1.010, albumin, sugar, acetone, and centrifuged sediment negative; complete blood count: red blood cell count, 3,200,000; hemoglobin, 9.4 Gm.; white blood count, 7,200; blood urea nitrogen, 27 mg. per cent.

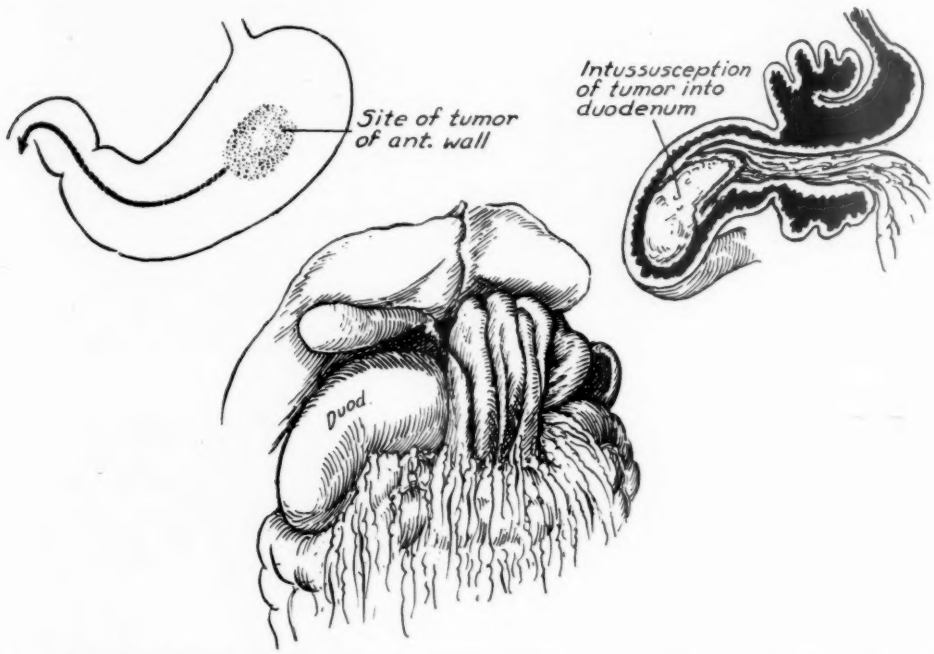
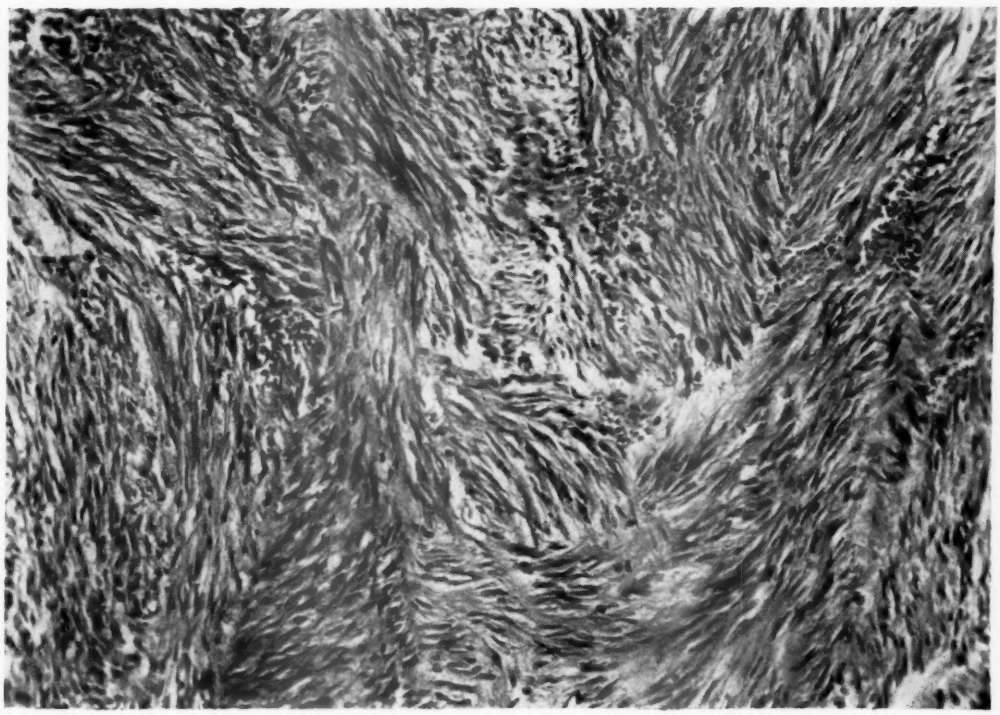


Fig. 2 (I. D., New York Hospital No. 580577).—Diagram illustrating position of the leiomyoma in the stomach, the condition encountered at exploratory celiotomy, and cross section of the intussusception prior to reduction.

Following admission, the patient was placed on complete rest in bed, and received 500 c.c. of blood as a supportive measure. On reviewing the x-ray pictures, the bizarre and quite bewildering pictures of the stomach and duodenum were interpreted by the staff as a tumor of the first or second part of the duodenum.

Because this patient had bled continuously for four days, and because there was roentgen evidence of serious pathologic changes in the upper gastrointestinal tract, he was subjected to exploratory celiotomy. The duodenum was over two times the normal width, and there seemed to be a tumor mass in the lumen extending from the pylorus distally for four inches. The stomach was completely contorted and, therefore, the greater curvature could only be identified for about six inches proximal to the pylorus. While the stomach was being freed for further examination, the whole tumor mass in the duodenum suddenly reduced itself into the stomach with a "snap," and the stomach reverted to normal contour. The diagnosis of previous gastroduodenal intussusception was then obvious (Fig. 2). A tumor mass could be palpated in the fundus of the stomach along the greater curvature, and at the base of this tumor mass was an extraluminal nubbin of

A.



B.

Fig. 3 (I. D., New York Hospital No. 580577).—*A*, Gross specimen after removal. Note the extramural nubbin of tumor at the base of the specimen. There is ulceration of the mucosa over a large area of the intragastric portion of the lesion. *B*, Photomicrograph of the tumor displaying typical whorls and bundles of smooth muscle fibers. There are no mitoses.

tissue 1 cm. in diameter. Frozen section of this mass quickly bore out the belief that it was a benign tumor. By local excision, a leiomyoma approximately 6 cm. in diameter was removed. The wound was then closed in layers (Fig. 3).

Pathology Report.*—The main tumor was barrel-shaped and 6 by 4 cm. The base of it was 3 cm. wide and was intimately attached to the gastric wall. There was an extraluminal projection measuring 3 by 3 by 2 cm. There was ulceration over the main portion of the tumor as well as of the adjoining gastric mucosa. On cross section, the tumor was brownish grey and of uniform, firm consistency. Microscopic examination revealed the tumor to be mesenchymal, unencapsulated, and replacing the gastric wall beneath the muscular layer of the stomach. There was moderate inflammation surrounding the tumor. The tumor itself was composed of compactly arranged bundles and cords of smooth muscle, the cells being compact and uniform in size, shape, and staining qualities.

The postoperative course was uneventful. Two further replacement transfusions were administered which completely corrected the anemia which existed when the patient was admitted. The blood urea nitrogen returned to normal after cessation of the gastrointestinal bleeding. The patient's urinary output was excellent. He was placed on a progressive gastric regimen and was taking a six-feeding soft diet by the seventh postoperative day. He was discharged to his home on the tenth day after operation. Since that time the patient has fared well. There has been no recurrence of abdominal pain, the blood count has remained within normal limits, and the patient eats an unrestricted diet; the bowels move regularly, and there has been no evidence of gastrointestinal bleeding. The wound has remained well healed, and gastrointestinal roentgenograms taken two years after operation revealed normal function of esophagus, stomach, and duodenum. The duodenum is of normal size. There is no abnormality of the fundus of the stomach.

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*Pathology report by Dr. John M. Pearce.

CONGENITAL ANGIOMATOUS MALFORMATION INVOLVING THE ENTIRE LOWER EXTREMITY

Report of Hemipelvectomy in a 25-day-old Infant

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CONGENITAL angiomatous malformations of extreme magnitude, comprising large areas of body surface with involvement of underlying muscle groups, have fortunately been infrequently encountered, and radical surgery in the form of quarterectomy or massive excision has apparently been employed sparingly. The treatment of the smaller angiomatous malformations is now rather well standardized, being directed toward improving the cosmetic result and preventing infection and ulceration. Attacks on these lesions are usually made early, as entire features may be destroyed by progression of the growth. Depending upon the type and anatomic location of the angioma, the surgeon has at his disposal an array of therapeutic agents including excission and primary closure, skin grafting, x-ray therapy, interstitial radiation, sclerosing agents, tattooing, freezing methods, multiple suture techniques, and stage resections. An excellent review relating to the classification and treatment of these congenital anomalies may be found in the article by Brown.[2]

For massive angiomatous malformations involving large areas of the body, conservative methods of therapy aimed at restoring diseased tissue to a useful function are at times disappointing, particularly if the muscle groups are seeded with the angiomatous network.

Recently, Ravitch[8] reported the successful performance of a hemipelvectomy in a 13-day-old infant with a massive hemolymphangioma involving the entire left lower extremity with a cystic extension of the deformity into the left lower abdominal quadrant. "It was felt that the limb was deformed beyond hope of redemption and that radical operation was justified to achieve a tolerable cosmetic result, to prevent ulceration and infection, and to check the growth of the malformation which notoriously extends into neighboring tissues and if allowed to progress, may actually threaten the life of the patient." Considering the extent to which the muscle groups of the extremity were involved in the angiomatous arrangement, it was felt that conservative therapy directed toward preserving the limb would prove useless.

Hemipelvectomy or hindquarter amputation has been performed with increasing frequency during the past decade.[1, 3-7, 10] With modern anesthesia, proper replacement therapy, and improved surgical technique, the operation is no longer viewed as an act of mutilation not within the armamentarium of a reputable surgeon.

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The indications for the procedure are now fairly well standardized and apply in the main to primary malignant osseous new growths involving the upper femoral shaft, the hip joint, and pelvic osseous structures. Also certain massive osseous neoplasms of a benign nature located in the above regions in which a more conservative type of surgical procedure would prove fruitless are best removed with sacroiliac disarticulation, either partial or complete. In

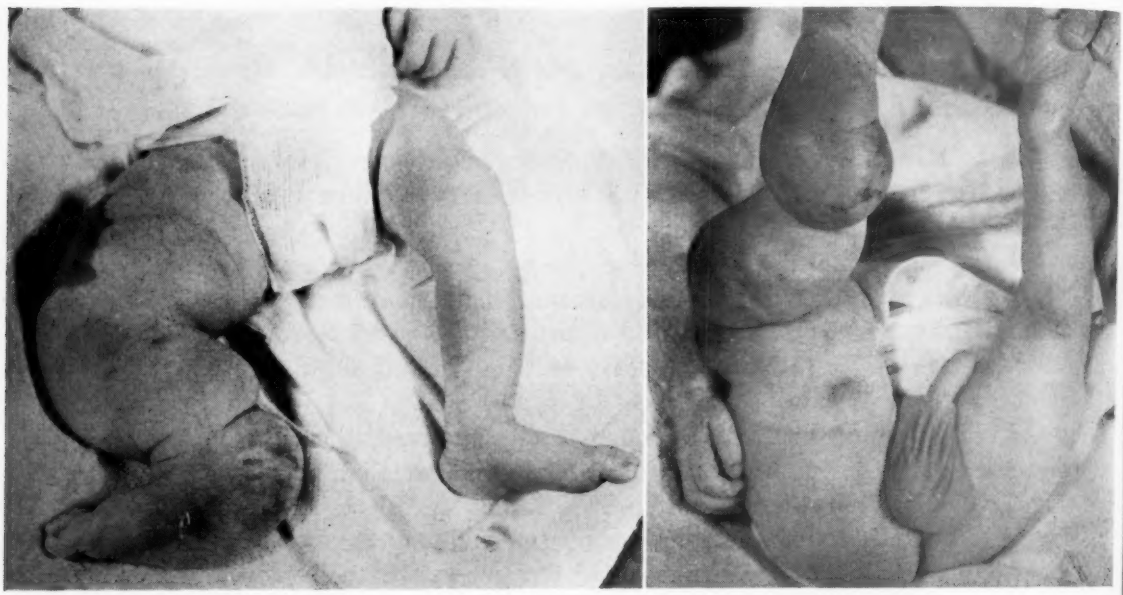


Fig. 1.—Photographs showing the extent of surface involvement by the malformation.

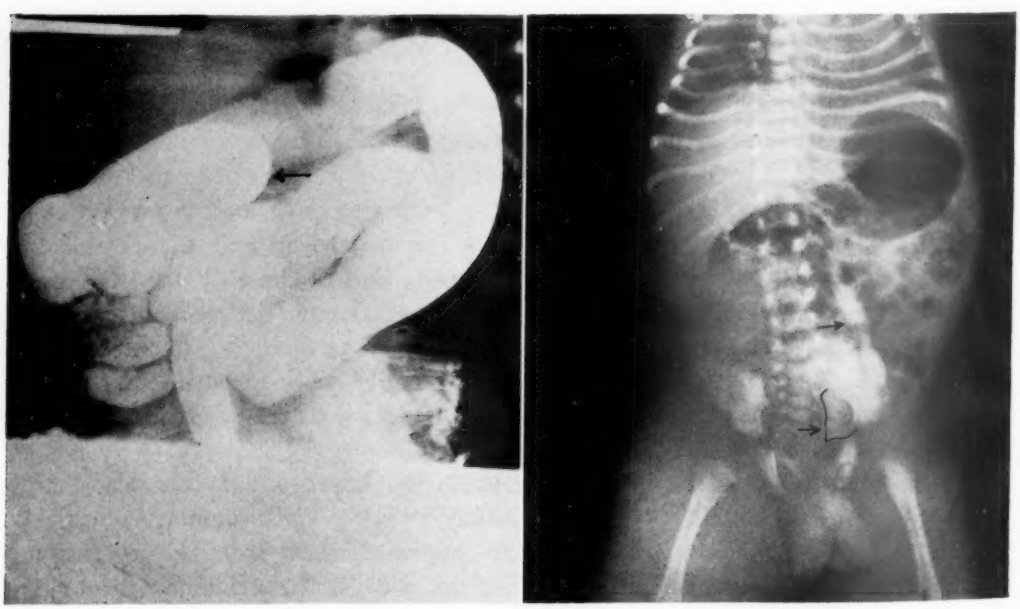


Fig. 2.—The cecum is displaced superiorly as demonstrated by barium enema. The bladder is pushed to the left, and the left ureter is quite dilated.

this latter type of lesion, it may be desirable to leave the wing of the ilium intact if not involved in the pathologic process, as this will tend toward a better cosmetic result. The procedure also has a broad usefulness in treating certain primary malignant tumors involving the soft parietes of the thigh, groin, and buttocks. At present, there exists some controversy as to whether so radical an operation has any place in the palliative treatment of advanced cancer.

Fig. 3.—Drawing revealing the extent of the retroperitoneal cystic mass.

Cumulative experience to date utilizing hemipelvectomy for the removal of primary malignant osseous tumors shows that best results are being obtained with the chondrosarcoma group, the osteogenic tumors yielding the poorest outlook.

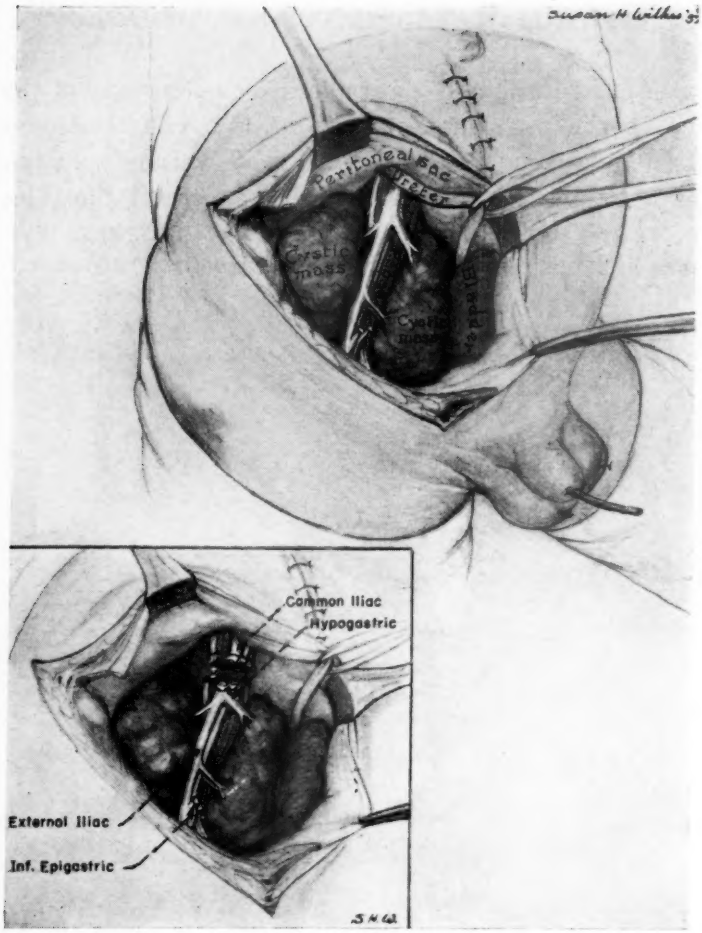


Fig. 4, *A*.

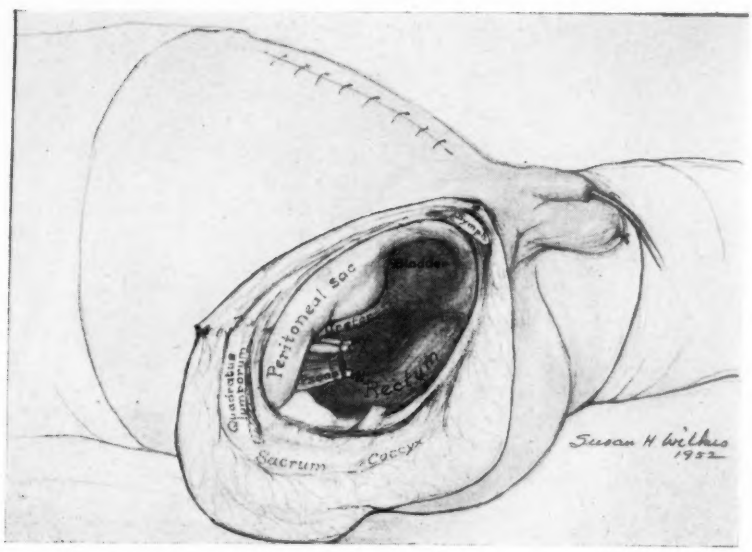


Fig. 4, *C*.

Fig. 4.—*A*, Shows the relationship of the retroperitoneal mass to the pelvic vessels. *B*, The gluteal muscle group almost entirely replaced by hemolymphangiomatous elements. *C*, Lateral view of pelvic structures following hindquarter removal. *D*, (Insert), Internal oblique muscle being approximated to the sacral fascia. Appearance of the wound at completion of the procedure.

Fig. 4, *B*. (*For legend, see opposite page.*)

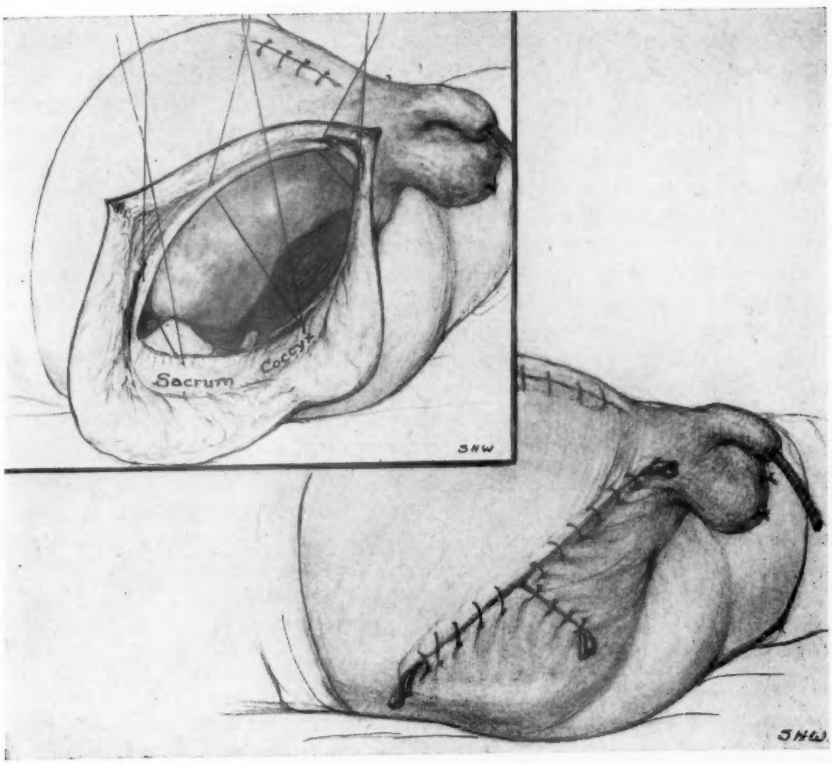


Fig. 4, *D*. (*For legend, see opposite page.*)

The purpose of this communication is to report the successful performance of a hemipelvectomy in a 25-day-old male infant who had a hemolymphangioma involving the entire right lower extremity and right buttock, with a cystic extension of the process into the right lower abdominal quadrant. This case was almost identical to the one reported by Ravitch except that the deformed limb of the infant upon whom he operated was perhaps a little more grotesque in appearance than the one to be reported.

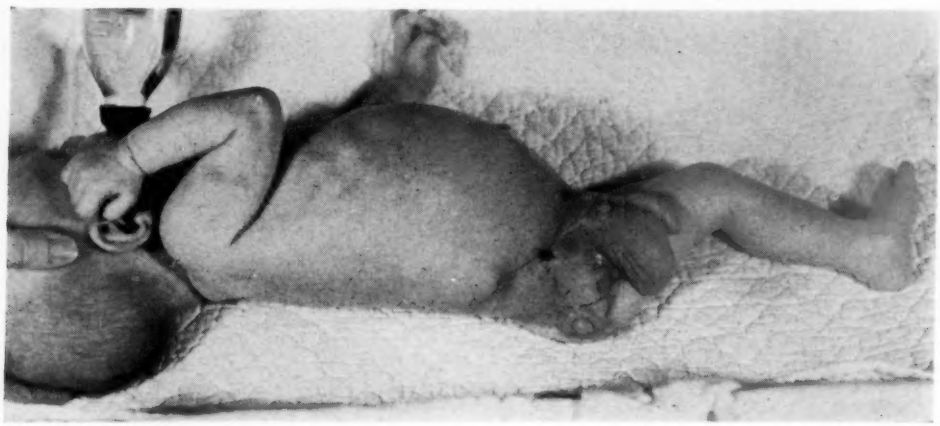


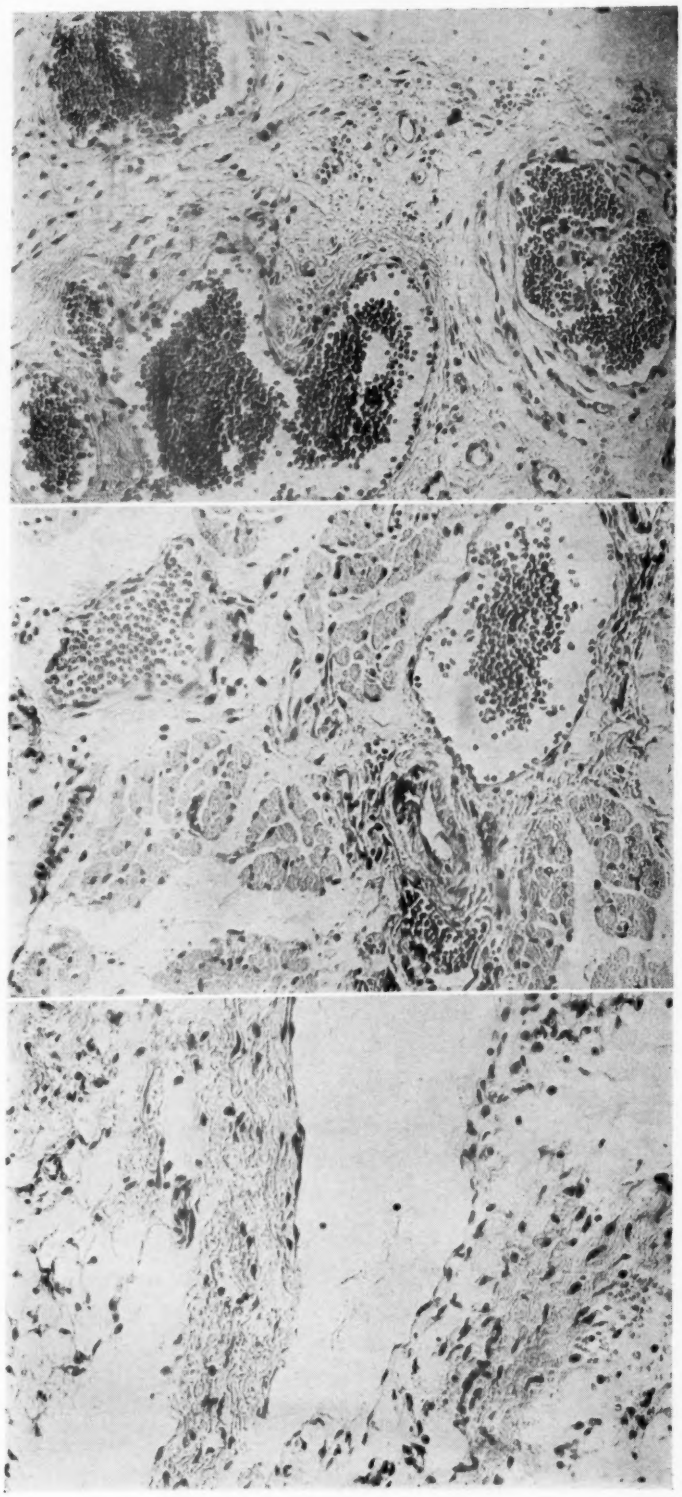
Fig. 5.—Appearance of the wound on the sixteenth postoperative day.

CASE REPORT

T. W. D. S. (Vanderbilt University Hospital No. 208061), a male infant, was born Feb. 16, 1952, at the Vanderbilt University Hospital, being the first offspring of normal parents. Birth weight was 8 pounds 7.75 ounces. Examination revealed an active-appearing male infant whose entire right lower extremity, extending from the foot to and including the right buttock was involved in a huge mass which appeared to represent a congenital hemangiomatous malformation. The skin over this extremity was discolored in several areas by the angiomatous elements with numerosu areas of telangiectasis. The extremity was several times larger than its counterpart, and the buttock was extensively involved in the process (Fig. 1). The tissues of the limb in areas were firm to palpation, giving the impression that the angiomatous elements extended into the underlying musculature. In a few areas, the underlying tissues felt cystic; this, no doubt, represented a lymphatic component to the malformation. In the right lower quadrant of the abdomen, an oval-shaped mass, apparently cystic in nature, could be easily palpated, and it measured approximately 5 by 5 cm. in diameter. It could likewise be felt on rectal examination and was thought to be retroperitoneal in location. Barium enema revealed that the cecum was displaced superiorly by the soft tissue mass, and intravenous urography showed the bladder and ureters to be pushed to the left (Fig. 2).

Since the involvement was so diffuse, it was felt that irradiation therapy or multiple stage resections would be of no avail. Also, from the physical examination alone, there was little doubt that most of the muscle groups of the extremity and buttock were infiltrated with the angiomatous process, thus rendering a conservative approach to the problem impractical. A hemipelvectomy was decided upon as the treatment of choice, and I was indebted to Ravitch for the sound approach he used in his similar problem, as it was closely followed in the case under discussion.

Operation.—On March 13, 1952 (the infant being 25 days of age), the abdomen was opened through a low right rectus incision. There was a bilocular cystic retroperitoneal mass overlying the pelvic vessels which was encroaching upon the right lateral wall of the bladder



A.

B.

C.

Fig. 6.—Photomicrographs ×150, reduced one-sixth. *A*, Dilated vascular channels of blood vascular origin located in the subcutaneous tissues. Note the increased amount of fibrous tissue present. *B*, Throughout the musculature, blood vessel channels are also noted. *C*, Dilated cystlike spaces, void of blood elements, are noted in the subcutaneous tissue. These apparently represent the lymphangiomatous component of the malformation.

(Fig. 3). The mass did not extend to the midline of the sacrum and did not rise above the brim of the pelvis. It was felt that it could be excised with the hindquarter amputation. Therefore, the abdomen was closed in layers with interrupted silk sutures.

Fig. 7.—Photograph of the infant at 10 months of age.

A hemipelvectomy was then carried out, using essentially the technique described by Ravitch (Fig. 4).[9] The cystic mass was approached by reflecting the peritoneal coat superiorly and was found to represent a cystic hygroma. This mass was inadvertently ruptured during the dissection, but was removed in its entirety. The anterior portion of the procedure entailed division of the tendinous attachment of the right rectus muscle at the pubis. The common iliac vessels were ligated, divided, and transfixed, rather than the external iliac vessels, as it was planned to sacrifice the greater portion of the skin of the buttock in the posterior part of the dissection; thus there was no cause to be concerned about the viability of the posterior skin flap. The division of the psoas muscle, femoral nerve, and pubic symphysis completed the anterior portion of the dissection. The posterior skin flap was then fashioned, and the structures divided posteriorly were the quadratus lumborum, gluteus maximus, and piriformis muscles, the sacrotuberous and sacrospinus ligaments, and the sciatic nerve. The muscles were infiltrated with angiomatous tissue. The sacroiliac joint was divided with the scalpel, and finally the ischiocavernosus and levator sling were severed. Bleeding throughout the procedure was minimal, and the estimated blood loss from weighed sponges totaled 220 c.c. Whole blood in the amount of 350 c.c. was administered slowly throughout the precedure. Closure of the wound was carried out by suturing the internal oblique muscle to the sacral fascia with interrupted fine silk. The subcutaneous tissues were easily approximated, and a small wedge of skin was removed from the central portion of the posterior flap as some redundancy was present. The skin was then closed with the wound assuming the final shape of the letter "T." A rubber drain was placed in all three angles of the wound.

Postoperative Course.—The infant did unusually well following the operation. There was no fall in blood pressure postoperatively and very little sanguineous drainage from the wound, the drains being removed in seventy-two hours. Forty-eight hours after operation he was taking a milk formula well and showed no signs of abdominal distention. There was no difficulty with voiding or defecation. Sutures were removed from both wounds on the ninth

postoperative day, and each had healed per primam. The baby did not develop any anemia during the hospital convalescence, and the hemoglobin value just prior to discharge was 16.3 Gm. He was discharged on the sixteenth postoperative day (Fig. 5).

Pathologic Report.—Microscopically the malformation consisted of dilated vascular channels throughout the subcutaneous tissues and musculature, primarily of blood vascular origin. In other areas endothelial lined spaces of apparent lymphangiomatous origin were also present, but to a lesser degree (Fig. 6).

Follow-up.—The infant has continued to develop normally in every respect. At six months of age the birth weight was practically doubled (16 lbs. 15 oz.). At the present time he is ten months of age, weighs 19 lbs. 6 oz., and there is no evidence of recurrence (Fig. 7).

SUMMARY

A 25-day-old infant was subjected to a hemipelvectomy for a massive, deforming hemolymphangioma involving the entire right lower extremity and right buttock with a hygromatous extension of the process into the right lower abdominal quadrant. Reasons for electing this method of treatment, rather than utilizing more conservative measures with the hope of salvaging the limb, have been presented.

During the ten months' follow-up there has been no evidence of recurrence and the infant has continued to develop normally.

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Editorial

Peptic Ulceration and Gastrointestinal Hemorrhage

SURGERY is merely a branch of medicine. Operation is only one of many alternative forms of treatment and, as it must of necessity involve some risk, discomfort, and temporary incapacity, it can be recommended only when no other form of treatment is available, when other treatments are more lengthy, more unpleasant, or more unsatisfactory, when other treatments are likely to fail, or when they have failed. Peptic ulceration is not necessarily a fatal or even a progressive disease; therefore, medical treatment must come first. I use the term "medical treatment" in its broadest sense, for the most important part of it is social and economic. I could cure all duodenal ulcers in their early stages without operation were I allowed to change the man's job and shoot his wife.

When has medical treatment failed? It has obviously failed when the ulcer has perforated, although that is the wrong way of putting it. The ulcers that perforate are usually acute ones with a history of under one week, and when they perforate they have had no treatment of any kind. What I mean is that in perforation the treatment is by operation.

There has been a lot of talk about the nonoperative treatment of perforation. It is foolish talk, and it has done a lot of harm because there are a lot of fools about who are apt to believe what they read. I am not claiming for a moment that an operation to close a perforation does much good. A perforation is an acute lesion. The edges of the hole are rotten edematous tissue. The stitches pull out unless they are tied so loosely that they do little more than approximate the edges. The repair of the hole depends, not on the stitches we put in at the time, but on the gastric contents we suck out afterward. If the stomach is kept empty by suction, the perforation will close whether it is sutured or not. The reason we operate is to remove the gastric contents that have flooded the peritoneum, the bits of meat, potato, cabbage, and carrot that inevitably bring a septic peritonitis on top of the chemical one if they are not removed.

It follows that there are perforations that do not need operation, those in which there has been minimal soiling, but they are few and their selection is a matter for a surgeon of considerable experience. They are those where a man, giving a typical history, arrives at a hospital two hours later looking and feeling well, with nothing but a little guarding under the liver to show that anything is amiss. An x-ray picture showing air under the diaphragm confirms the diagnosis. Such patients do better if treated by suction and chemotherapy than if submitted to operation.

Second, medical treatment has failed if the ulcer has gone on to stenosis, either duodenal or mid-gastric. There is no such thing as pyloric stenosis, except in infancy. Here we must operate or the patient will starve to death.

Third, medical treatment has failed when repeated attacks of severe bleeding endanger life. This question of hemorrhage we shall consider later.

When is medical treatment likely to fail? That is a very difficult question to answer, but let us take the three absolute indications, perforation, stenosis, and major hemorrhage. Most perforations, once recovered, are never heard of again, but we do meet unfortunate patients, usually young, in whom perforation occurs again and again. When a man has perforated twice, he should have a radical operation that will cure the ulcer and the ulcer diathesis, and make him safe for the future, but he should not have it at the time. We shall damage surgery and fail in our duty to our patients if we abandon the simple outlook that in an emergency it is our duty to right the emergency as quickly and as simply as possible, and nothing more.

Stenosis is partial long before it becomes absolute. If vomiting is becoming an increasingly prominent feature of the clinical history, if x-ray pictures show an increasing delay in emptying, if when examining the patient we find a succussion splash more than two hours after his last drink, then stenosis sufficiently severe to lead to malnutrition is not far off, and it is our duty to advise operation. Similarly with hemorrhage, a loss of blood sufficiently severe to make a man feel dizzy and to bring the hemoglobin down to sixty, even if it stops quickly and does not require transfusion, is a warning. If it is repeated more than once in three years, it means that an artery large enough to bleed fatally next time is lying in the base of the ulcer, somewhat insecurely covered by fibrous tissue.

But the most common indication of the impending failure of medical treatment is pain, increasing in frequency and severity in spite of medical treatment conscientiously followed. In that group, described by Alvarez as being of poor personal material, medical treatment fails because the patient is a failure, his life is a failure, his job is a failure, his marriage is a failure, his stomach has let him down, and he pursues medical treatment with mournful and despondent irregularity to the inevitable failure that he expects. The patients of unsatisfactory moral fiber are not going to be a credit to surgery.

On the other hand, the man who obeys instructions and leads a reasonable life, yet at the age of 45 or 50 years can keep the ulcer quiet only by sticking to a strictly limited diet, must face the choice between a life becoming more and more restricted and an operation. In such a case, we can unhesitatingly advise surgery.

Here we must face the usual question of the heckler. What magic is there in numbers? Why recommend operation only after 45? Why not 40? Why not 30? Why not 20? If the results of operation are as good as they seem to be, why not give all ulcer sufferers the benefit of freedom from pain and of a carefree existence after trying a short course of medical treatment?

The answer involves the consideration of the difference between gastric and duodenal ulcer. We know nothing of the cause of gastric ulcer, but we do know that the causes of persistence are in the stomach itself. The stomach is a distensible bag, coupled in tandem to a muscular mill, containing a highly destructive fluid, and lined with a continuous film of mucus that protects its walls from digestion. Once the stomach has become fixed to neighboring organs, once the smooth flow of its muscular contractions is interrupted by a fibrous gap, once the protecting sheet of mucus is interrupted by a patch of single-layer epithelium, nothing better than temporary healing of an ulcer can be expected. Whatever the age, the time for gastrectomy has come.

We know quite a lot about the cause of duodenal ulcer, or we think we do. In southern England, at any rate, duodenal ulcer seems to be the local manifestation of an anxious frustrated make-up in which overwork, worry, hope deferred, irregular meals, loneliness, and excessive cigarette smoking all play their part. If the "duodenal diathesis" (I put this in quotation marks) can be alleviated or corrected, the ulcer, unless it has already caused too much destruction, will heal and remain healed. The duodenum is not a reservoir or a mill, but a passageway. It is not bathed in acid, for in a properly functioning gastric mechanism nothing is allowed out of the pylorus until it has been neutralized by an alkaline pyloric secretion, and any acid that does escape is looked after by Brunner's glands. Therefore, a healed and scarred duodenum can still do its job perfectly well. Surgery is reserved for the treatment of complications.

The surgical treatment of duodenal ulcer involves a severe and, still more important, a most profoundly multilating operation, undertaken with the sole object of reducing the acid secretions of the stomach to a level at which reulceration cannot take place, and of limiting this secretion to the time that food is in the stomach. Anything less is courting failure. The operation abolishes many things on which normal health and normal nutrition depend. It abolishes almost completely the reservoir in which food is stored while it undergoes preliminary digestion. It abolishes the pylorus and, with it, any control of the time during which food is retained in the stomach. It abolishes the greater part of the mechanism for digesting meat fibers. It abolishes largely the guard against the entry of swallowed bacteria. It abolishes the normal mechanism whereby the biliary and pancreatic secretions are called up. After gastrectomy, much of the protein and fat in the diet is passed on unaltered. The patients usually remain lean. The amazing thing after such sabotage is that gastrectomy, properly performed, is sensationally successful. The patients, after years of misery, are riotously happy, and they go the round of restaurants for the mere pleasure of pouring down their esophagus all the good things whose taste they have almost forgotten. We know that they keep well for ten or twenty years, but do we know that they will remain well for forty, fifty, or sixty years? We occasionally find strange nutritional anemias developing. We occasionally get an old dormant pulmonary tuberculosis lighting up. It is a fear that dietary deficiencies which are not clinically ap-

parent may exert a cumulative effect as the years go by that makes me fear to perform gastrectomy in a patient under the age of 40 years, unless I am forced to do so.

I am referring to gastrectomy as the treatment, indeed the only satisfactory treatment at the present time, of peptic ulceration requiring surgery. I would most earnestly urge you to accept this standpoint. Something better may come tomorrow; there is nothing better today, and several treatments are very much worse.

Vasoligation is shocking, and its originators should be thoroughly ashamed of it. They may be, but I have waited in vain for a public repentance. Had they been frank about its failure, fewer foolish young men would have followed them along this disastrous path. Vagotomy is more rational, but not much more successful, and Dragstedt, although he has not apologized, is doing very much the same thing by spending most of his time defending his baby from the attacks of fellow Americans. Gastrojejunostomy is on a different footing, for it is a well-designed operation with a long and honorable history, and it does overcome stenosis. Unfortunately, it was based on mistaken physiology. It leaves the late-appearing hormonic wave of acid secretion untouched, and it is followed eventually by jejunal ulceration in at least 20 per cent of cases.

It is often urged, "but these operations are easier and, therefore, safer for the beginner." Is the health of the nation to be at the mercies of beginners? The operative treatment is, in most cases, one of the utmost simplicity, raised by box-office ballyhoo to the level of a popular crooner. Apart from the surgery of access, which is usually performed by a resident before the surgeon arrives, the operation is a glorified rectal examination. It requires practice and skill, but gastrectomy requires more practice and more skill; yet, it is handed over to beginners without supervision. I say this with some feeling, because we still see far too many bad results of gastric surgery, and the bad results of gastric surgery are, with few exceptions, the results of bad gastric surgery. The mortality should not exceed 1 per cent. There should be no recurrent ulcers. There should be no dumping syndrome or proximal loop regurgitation. Most of the patients should be perfectly well, and all should be glad that they had the operation performed. An interesting side light on the not entirely satisfactory results of gastrectomy was thrown by a follow-up in a large hospital. As a yardstick, the surgeon conducted the same questionnaire and examination on 200 patients from the fracture clinic. He found that 30 per cent of them, had they had a gastrectomy, would have been classed as "not entirely satisfactory."

By gastrointestinal hemorrhage I mean hemorrhage poured into the stomach, that is, hemorrhage arising in the divisions of the celiac axis artery or its branches, or in the corresponding branches of the portal vein. Such hemorrhage may appear as hematemesis, as melena, or as both.

Hurst confused this subject for a generation by discussing all cases of hematemesis together, without regard to their severity. There are two distinct problems, hemorrhage from an inflamed surface, and hemorrhage from

a large vessel. Hemorrhage from an inflamed surface occurs whenever an ulcer is active. It is seldom profuse but, if continued, it may lead to profound anemia. The treatment is, in the first place, medical. Hemorrhage from a large vessel may be exsanguinating, and can be fatal within the course of a few hours. In discussing treatment, surgery must always be seriously considered.

In the case of hemorrhage from a chronic ulcer, I think we have reached an agreed outlook, largely owing to the teaching and influence of Gordon-Taylor. If the lesion has been demonstrated previously, if the patient is 50 years old, and if after forty-eight hours blood loss continues, operation must be undertaken as an emergency measure. A history of previous severe hemorrhage would justify operation in a younger patient and at an earlier stage.

I will deal with two single points, hematemesis from an unknown source, and hematemesis in portal hypertension.

The surgeon may be forced to operation for hematemesis even in the absence of a demonstrable lesion, because the hemorrhage shows no sign of abating, and the patient is losing ground in spite of massive transfusion. Having opened the abdomen, he satisfies himself that blood is, in fact, coming from the upper reaches and not from lower down. If the bleeding is duodenal, he will feel the ulcer. If the bleeding is from esophageal varices, he will see that other branches of the portal vein are obviously enlarged. If he finds neither, I believe that he should do a gastrectomy, for the blood is always coming from a gastric ulcer. I have within the past year done such a "blind" gastrectomy five times, and in each case, when the duodenum has been divided and the stomach lifted up, I have found an ulcer that I had been unable to see or feel before.

Bleeding from esophageal varices raises the whole question of the surgery of portal hypertension. I know of no branch of surgery more urgently in need of debunking. In making a splenorenal or portocaval anastomosis, the surgeon divides a number of natural anastomoses whose total cross section is much greater than that of the rather poor one he is about to construct. The subsequent history of patients who have undergone these operations is, on the average, no better than that of those who have been untreated and, when they die, the new opening is usually found to have closed. When the operation is undertaken for severe hematemesis, the simplest procedure that will stop the bleeding and make fresh bleeding unlikely is clearly the right one. Such an operation is splenectomy combined with division of the left gastric pedicle. This safe and simple operation interrupts all the vessels bringing portal blood to the esophagus along the greater and lesser curvatures of the stomach. In my experience, which is admittedly small, it has stopped the hemorrhage and prevented further attacks.

—*Sir Heneage Ogilvie*

Recent Advances in Surgery

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THORACOABDOMINAL INCISIONS

A REVIEW

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(From the Department of Surgery, University of Michigan)

AS SURGERY widened its scope, it was inevitable that lesions in the upper abdomen and in the lower thorax could be more readily approached for definitive treatment by an incision that gave exposure to both of these cavities. Such incisions have widened considerably the surgeon's attack upon the lower esophagus, stomach, transverse colon, spleen, liver, diaphragm, kidney, and adrenal gland. In the surgery of trauma, the thoracoabdominal incision has been most useful in patients with penetrating lesions of both the thorax and the abdomen. Such an exposure enables the surgeon to explore almost the entire extent of both serous cavities for injury. Simultaneous advances in anesthesia have helped to dissipate the early fears of entering the pleural and peritoneal cavities simultaneously. During the past fifteen years and principally during the last decade, many surgeons have devised a variety of techniques of thoracoabdominal incisions. While they all accomplish the same purpose, the methods of approach vary. The present discussion will trace the development of the thoracoabdominal incisions and describe the various techniques in use today.

INCISIONS DEVELOPED PRIOR TO 1942

Attempts at devising a better approach to the upper abdominal contents date back to the last decade of the nineteenth century. During this period of surgery, and for many years thereafter, there was great fear of entering the pleural cavity, and many complicated osteochondral-flap procedures were devised, all directed to avoid entering the pleural space. Most of the incisions were developed primarily to obtain a wider exposure for operations upon the cardia of the stomach. Lannelongue and Micheli can rightfully be termed the co-founders of the combined thoracoabdominal incision, although they never actually performed their procedures on living persons. Lannelongue[19] described in 1895 a method for entering the subphrenic space and for reaching the convexity of the liver in order to expose hepatic cysts and abscesses. He recommended incising the eighth to the eleventh ribs or cartilages, maintaining the integrity of the pleura and creating a large flap which he turned

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cephalad. An actual description of this procedure is not recorded. Also in 1895 Micheli[22] described a procedure producing a large extrapleural thoracoabdominal flap by incising the abdominal wall, the thoracic wall, the ribs, and intercostal spaces along the costal margin. He, like Lannelongue, never had the opportunity to attempt this procedure on a living person.

Perhaps under the stimulation of the suggestions of Lannelongue and Micheli, von Mikulicz[23] performed in 1896 the first actual recorded procedure of this type. He resected a carcinoma of the lower esophagus and cardia utilizing an incision patterned after that of Micheli. His procedure was specifically designed to avoid entering the pleural cavity and, to prevent this, von Mikulicz obliterated the costodiaphragmatic space by suturing together the thoracic wall, costal pleura, and diaphragmatic pleura. The initial incision was a midline vertical incision extending from the xyphoid cartilage to the umbilicus. It was extended horizontally to the left costal margin and, from there, perpendicularly upward. An extrapleural costochondral flap was thus formed. The patient died shortly after the completion of the operation. In 1899 von Mikulicz again resected a carcinoma of the esophagus and cardia, but utilized a slightly different approach. After the primary abdominal incision from the ensiform cartilage to the umbilicus, a second incision was made perpendicular to the first at the level of the seventh costal cartilage and carried laterally to the anterior axillary line. The costochondral junctions of the seventh, eighth, and ninth ribs were transected, and, by retracting the ribs laterally, the cardia was visualized. This patient also died shortly after the operation was completed.

It was not until 1903 that the next attempt at a combined thoracoabdominal incision was made. In that year, Marwedel,[21] after seven and one-half years' work on cadavers, employed a combined incision in operating upon a stenosis of the lower esophagus. His approach followed the costal margin and was entirely extrapleural. A left curved incision was made two fingerbreadths below the costal margin and parallel to it. This extended from the ensiform cartilage to the tenth rib. The third to the seventh costal cartilages were transected; the rectus abdominis and the external oblique muscles were detached from their cartilaginous attachments, and the costochondral junctions of the seventh, eighth, and ninth ribs were cut through. The thoracic cage was retracted upward, thereby exposing the left upper quadrant of the abdomen. This procedure completely destroyed the left costal margin.

In 1905 Sauerbruck[29] proposed a technique which consisted of a transthoracic mobilization of the lower esophagus which was then invaginated through the cardia into the stomach. A laparotomy was later performed and the invaginated portion removed through an opening in the stomach. He never performed this procedure on a living person.

Tiegel[31] in 1909 reported a case of Henle's in which a thoracoabdominal approach in two stages was performed for a carcinoma of the stomach. Through the initial incision the stomach was mobilized and transected below the tumor. The resected portion was closed and a Murphy button was placed in the distal opening. The abdomen was closed and a left thoracotomy was

performed transpleurally. The esophagus was severed above the tumor and the anastomosis was accomplished with the Murphy button. The patient withstood the procedure, but died several hours postoperatively from atelectasis of the left lung.

Also in 1909 Wendel[34] performed a similar operation except that the thoracotomy was the primary procedure. He discovered a tumor involving the posterior wall of the esophagus which extended above and below the diaphragm. The esophagus was divided above the tumor and the proximal end was brought out through the thoracotomy incision. The distal end of the esophagus was closed and the thoracotomy incision sutured. Through an abdominal incision, the tumor was resected and the opening in the distal end of the stomach was left as a permanent gastrostomy. The patient died twenty-four hours postoperatively from a massive left hemothorax.

Janeway and Green,[15] after working on dogs and cadavers, devised in 1910 a two-incision thoracoabdominal technique. Through a primary abdominal incision in the midline of the upper abdomen, the stomach was mobilized, after which the wound was closed. The subject was turned on its right side, and a thoracotomy was performed through the bed of the eighth rib. The left crus of the diaphragm was incised and the stomach, previously freed, was delivered into the chest. Janeway performed this procedure on one patient successfully. He resected a carcinoma of the lower esophagus. The patient died fifty-four hours postoperatively from acute empyema resulting from a leak at the anastomosis site. On the basis of this limited experience, Janeway suggested a thoracoabdominal approach by a single incision. He postulated that an incision extending from the posterior axillary line through the bed of the eighth rib, crossing the costal margin, and proceeding obliquely to the umbilicus would provide a much wider visualization of the left upper quadrant and lower esophagus (Fig. 1, *A*). He recommended that the chest not be opened until all of the abdominal dissection was completed. Janeway never had the opportunity to use this approach surgically.

Zaaijer[36] in 1911 performed a two-stage resection for carcinoma of the lower esophagus. A gastrostomy was first performed and was followed by a one-stage thoracoplasty, removing the sixth to the eleventh ribs on the left side. This allowed the chest to fall in, thereby shortening the distance between the esophagus and the skin margins. A few weeks later, the second stage was performed which consisted of an incision beginning in the lower left hypochondrium at the mammary line. This incision extended to the posterior axillary line, and, from there, to the inferior angle of the scapula. The thoracic and abdominal cavities were opened and the diaphragm was severed. The distal end of the esophagus and the cardia of the stomach were resected. The proximal end of the esophagus was brought out to the skin margin in the thoracic wound and the distal stomach opening was closed. The patient recovered from the operation, but died of inanition in three months.

The approach suggested by Janeway went unheeded until Kirschner[16] in 1920 employed a similar incision for a resection of the lower esophagus.

With the patient placed on the side, he began his incision at the junction of the proximal and middle thirds of a line between the xyphoid process and the umbilicus. He extended it obliquely downward and lateralward to the left costal margin, then across the costal margin and through the seventh intercostal space to the angle of the scapula. The diaphragm was incised to the esophageal hiatus. As will be noted later, this approach is very similar to those in use today.

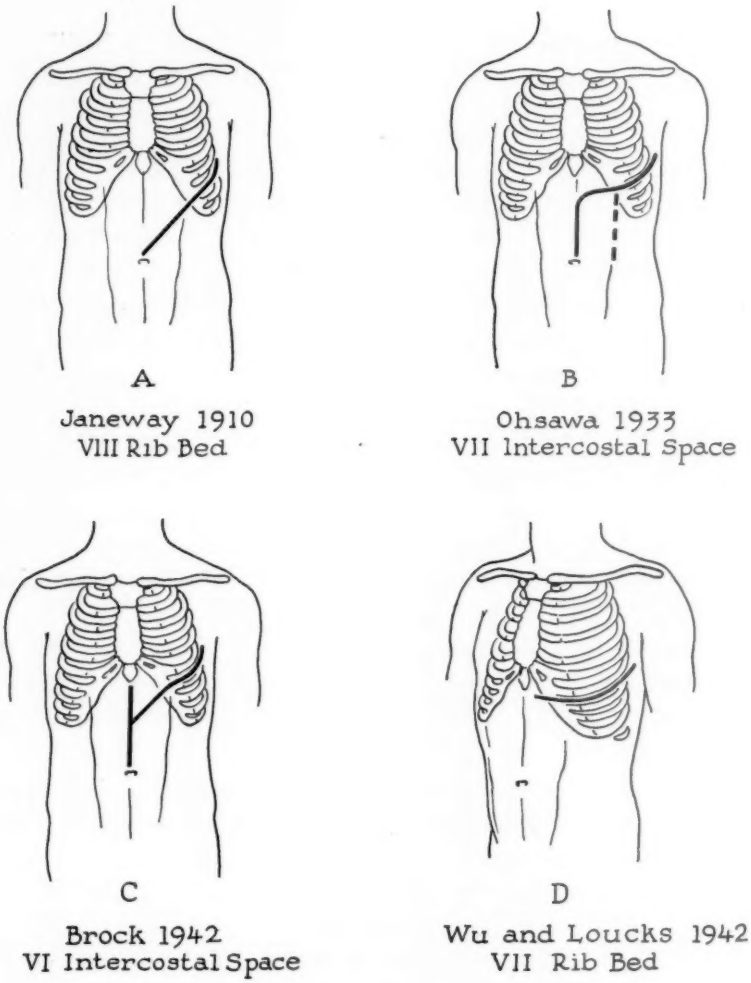

Fig. 1.—Incisions developed prior to 1942.

The first attempt at a single incision thoracoabdominal approach in the United States was performed for a carcinoma of the gastric cardia by Hedblom[13] in 1922. His procedure was a two-stage affair patterned after Zaaijer. On April 7, 11, and 14, 1922, thoracoplasties were performed resecting the fifth to the eleventh ribs from their angles to the costal margin. On May 15, 1922, the tumor was resected through an incision extending from the left of the midline just below the costal margin, upward and outward to the anterior

axillary line. After the peritoneum was opened and the tumor was found to be resectable, Hedblom enlarged his incision upward to the level of the fourth rib in the midaxillary line. The pleural cavity was entered and the diaphragm was incised to the esophageal hiatus. After removal of the tumor, Hedblom found he was unable to accomplish the esophagogastrostomy below the diaphragm. He, therefore, brought both ends to the outside creating an esophagostomy and a gastrostomy. These were later connected by a rubber tube. The patient survived the procedure and appeared quite well at the time of Hedblom's report several months later. He subsequently became very despondent and committed suicide.[26]

The first series of patients operated upon employing a combined approach for tumors of the lower esophagus and cardia of the stomach was reported by Ohsawa[25] in 1933 from Japan. He had eight survivals in eighteen attempts. He employed two types of incisions: the semithoracic transabdominal technique using Marwedel's left costal release, and a free thoracoabdominal technique patterned after Janeway and Kirschner. In the former technique an inverted U-shaped skin incision was made in the left upper quadrant producing a musculocutaneous flap which exposed the left upper abdominal muscles and the left lower ribs anteriorly. Portions of the seventh, eighth, and ninth ribs or their cartilages were resected 8 to 10 cm. from the midline. The ninth intercostal space was incised, and the costal attachment of the seventh rib was divided. The left costal margin was thus freed and then retracted. Ohsawa was able to expose the lower 10 cm. of the esophagus through this incision without entering the pleural cavity. His second approach consisted of a midline or a left pararectus abdominal incision extending from the level of the seventh costal cartilage to the umbilicus (Fig. 1, *B*). After a preliminary inspection of the abdominal viscera, the incision was carried upward and lateralward across the costal margin to the angle of the scapula. Segments of the seventh and eighth ribs were removed in most cases. The pleura was divided and the diaphragm incised to the hiatus, thus creating a single operative field. Ohsawa's operation was condemned by American surgeons because of its magnitude, and the development of a satisfactory thoracoabdominal incision was again delayed.

Garlock[7] in 1941 suggested a primary abdominal inspection followed by resection through the chest. He entered the abdominal cavity through an upper left rectus incision and, after exploration showed the lesion to be favorable for resection, he closed the abdominal wound with through-and-through steel wire. The chest was then opened through the eighth intercostal space, the seventh and eighth ribs being transected at their distal ends. His reason for advocating the preliminary abdominal incision was his belief that the lymphatic spread of carcinoma of the cardia was most often in a peripheral direction below the diaphragm and that only through a primary abdominal incision could operability be determined.

Brock[2] in 1942 reported the first successful esophagogastrostomy for carcinoma of the stomach from Europe. He employed a thoracoabdominal in-

cision quite by accident. After opening the abdomen through a vertical supraumbilical incision and removing the lesion, he discovered that he was unable to perform the anastomosis below the diaphragm. To effect this, he extended his incision from the middle of the abdominal wound into the sixth interspace (Fig. 1, *C*), incising the costal margin and separating the diaphragm from the costal margin. After performing this procedure successfully, Brock suggested that a single oblique incision along the same pathway would be just as effective.

From Peiping, China, in 1942, Wu and Loucks[35] reported seven cases of carcinoma of the lower esophagus and cardia of the stomach treated by primary resection and anastomosis through a combined incision. Their line of incision extended from the interscapular region along the seventh rib into the left hypochondrium, terminating at the lateral border of the left rectus muscle (Fig. 1, *D*). The entire seventh rib was removed and the chest was entered through its bed. The costal margin was then divided and the peritoneal cavity was entered. The diaphragm was incised to the esophageal hiatus with the production of a single pleural-peritoneal cavity.

INCISIONS DEVELOPED AFTER 1942

At the conclusion of World War II, the advances in anesthesia, the use of new antibiotics, and the experience gained in combat surgery all provided a great impetus for the further development of an adequate right and left thoracoabdominal incision. Since these approaches are in use today, most of them will be described here. Even though they all accomplish much the same purpose, that of increased exposure, they differ sufficiently to make a detailed description a necessity.

Garlock[9] in 1946 discarded his previously advised two-stage technique in favor of a single incision method, but still maintained that abdominal exploration should always be performed first in order to determine operability. His present technique is as follows: The patient is placed on the table on his right side in such a fashion as to incline his back toward the operating table at about five degrees beyond the exact lateral position. The left arm is supported toward the right side, thus swinging the scapula forward. The abdomen is entered through a left pararectus incision (Fig. 2, *A*). After determining resectability, the incision is extended to the costal margin and lateralward in the eighth interspace to the vertebral border of the scapula. The pleura is incised beginning close to the costal margin. The costal margin is transected as is also the diaphragm as far as the esophageal hiatus. Much less postoperative discomfort is claimed without rib resection. Garlock states that this type of incision accomplishes the following: (1) all manipulations are performed under direct vision, (2) the left gastric artery may be ligated at its origin, helping to insure adequate lymph node removal, (3) the incision enables the surgeon to resect more easily the spleen and tail of the pancreas if such becomes necessary, (4) it shortens the operating time, (5) in total gastrectomy, it provides an easier anastomosis.

Humphreys[14] devised a thoracoabdominal incision differing from Garlock only by the abdominal approach. The incision is begun just to the right of the midline about two inches above the umbilicus and is extended obliquely to the eighth costal cartilage (Fig. 2, *B*). After primary abdominal exploration, the incision is extended to the posterior axillary line in the eighth interspace. A routine rib resection is not performed.

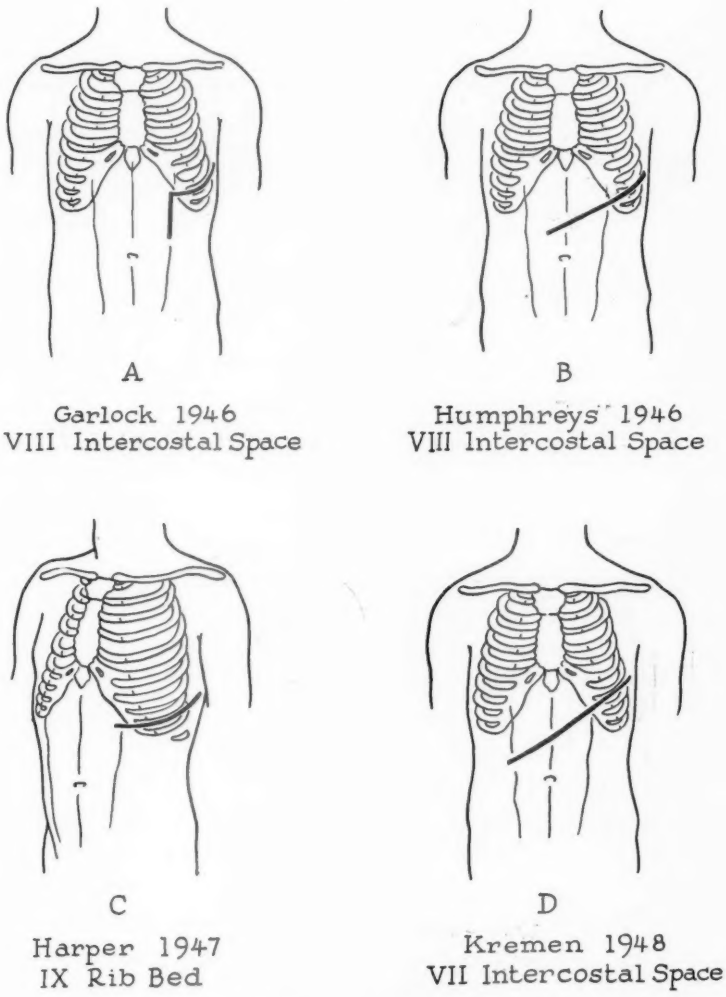

Fig. 2, *A.-D.*—Incisions developed after 1942.

Harper's[11] contribution of a thoracoabdominal incision is primarily a transthoracic approach with a short abdominal extension (Fig. 2, *C*). His wound extends through the bed of the ninth rib, across the costal margin, and into the abdomen for a distance of approximately two inches. The diaphragm is incised to the esophageal hiatus.

Kremen,[17] realizing that most of the dissection in a total gastrectomy and esophagogastrectomy takes place in the abdomen, claimed that his incision was devised for the surgeon who is more at home in the abdomen. The patient is

placed supine on the table with a sandbag under his left side. This produces an elevation of about ten degrees. The abdomen is entered through a horizontal and upward incision begun at the lateral border of the right rectus muscle, just above the umbilicus. It is carried to the eighth costal cartilage at the seventh intercostal space (Fig. 2, *D*). After abdominal exploration the table is rotated and the patient is elevated to twenty to twenty-five degrees.

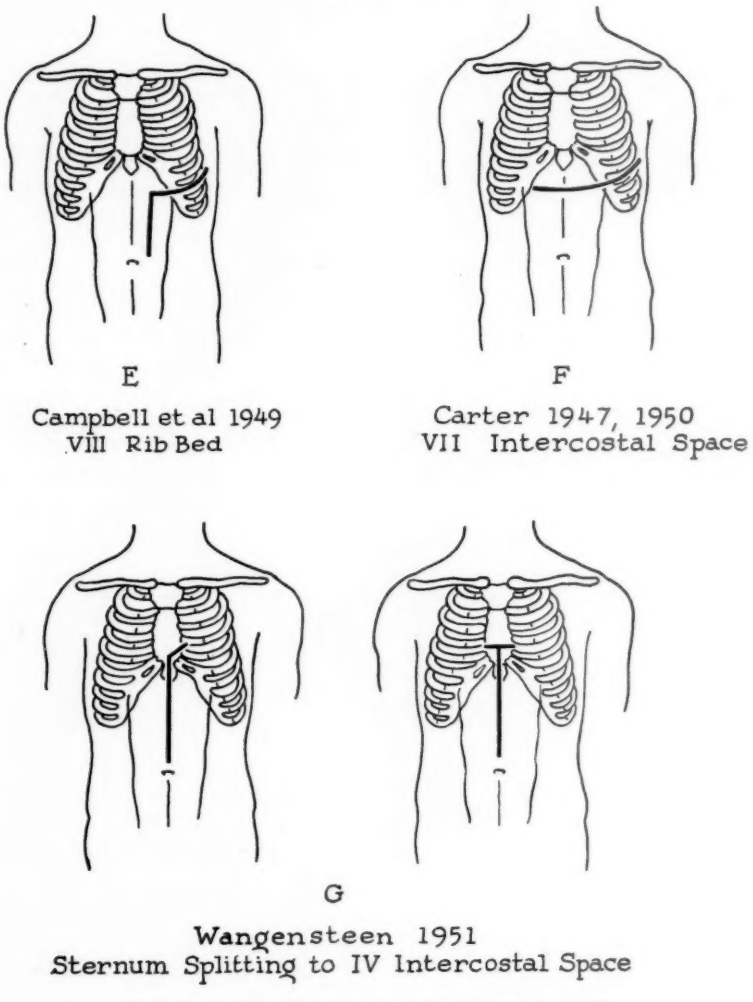

Fig. 2, *E.-G.*—Incisions developed after 1942.

The chest is opened by incising the eighth costal cartilage and the seventh intercostal space to the posterior axillary line. If an infradiaphragmatic anastomosis is performed, the diaphragm is incised only halfway to the hiatus. For a supradiaphragmatic anastomosis the diaphragm is transected to the hiatus. This incision of Kremen's differs only in the interspace entered from that described by Humphreys.

Campbell, Alexander, and Mikal[3] have used a left rectus incision extending from the seventh costal cartilage to the umbilicus. After routine ab-

dominal exploration, the incision is carried along the seventh or eighth rib to the interscapular area (Fig. 2, *E*). The chosen rib is resected and the pleural cavity entered through the rib bed. The diaphragm is incised to the esophageal hiatus.

Carter's[4] incision has probably gained the most popularity, especially from those surgeons who are proponents of the transverse abdominal incision. It is especially adaptable for prolonging an inadequate transverse upper abdominal incision. A transverse incision is made midway between the xyphoid process and the umbilicus, transecting, usually, both recti muscles. It is prolonged into the left chest across the eighth costal cartilage and through the eighth interspace to the midscapular line (Fig. 2, *F*). The abdominal and thoracic muscles are transected in the line of the skin incision. The peritoneum is opened first, followed by transection of the costal margin and incision of the pleura. The diaphragm is incised from its attachment to the costal margin to the posterior angle of the wound. In 1950, Carter and Helmsworth,[5] after more experience with this approach, modified Carter's original incision somewhat. The incision is now carried only to the posterior axillary line instead of to the mid-scapular line. For esophageal lesions, the seventh intercostal space is utilized. For operations upon the spleen, liver, and kidney, the diaphragm is incised in the line of the skin incision; but for operations upon the stomach and esophagus, the diaphragm is transected to the esophageal hiatus. For high esophageal lesions, the incision is carried backward to the spine, and segments of the ribs above and below may be removed for better exposure.

Wangensteen[33] has employed for many years either a curved upper abdominal transverse incision or a modified curved incision with a midline vertical component for all operations upon the stomach. At the present time a sternotomy with a midline supraumbilical incision is rapidly replacing his former transverse approach. The sternum is divided extrapleurally in the midline, and the incision is curved into the left fourth or fifth intercostal space which provides excellent exposure of the upper abdominal viscera (Fig. 2, *G*). The xyphoid process is usually removed and discarded. Further exposure may be accomplished if a T bar is simultaneously made at the upper end of the divided sternum extrapleurally into the corresponding right intercostal space (Fig. 2, *G*). This incision then provides maximum exposure to the upper margins of the liver, the vena cava, and hepatic veins. If necessary the pericardium may be opened extrapleurally in order to control the intrapericardial portion of the vena cava before attacking the hepatic veins in right hepatic excision. The diaphragm may or may not be incised in the line of the incision. The exposure that one is able to obtain through this sternotomy incision is excellent for the lower esophagus and cardia of the stomach. Wangensteen has not as yet published any large series in which this incision has been employed.

Longmire[20] in a recent editorial on esophageal bleeding revived one of the earliest of incisions in performing portacaval or splenorenal anastomoses. He employs a long right or left diagonal incision over the costal margin with

transection of the costal margin and the ends of the sixth, seventh and eighth ribs. A costal margin flap is thus formed which is retracted upward. This is an extrapleural approach to the upper abdominal structures. Von Mikulicz and Marwedel utilized a similar approach.

Carter and Helmsworth[5] employed the thoracoabdominal incision in forty-three cases. The late complications included two cases of an unstable costal margin (Carter now approximates the costal margin with steel wire), and one case each of diaphragmatic hernia and a restricted diaphragm.

Mosely,[24] discussing the use of a combined approach in ten cases, stated that it is the easiest approach to the spleen, stomach, adrenal gland, and the thoracic duct. He has employed it in nephrectomy for large, fixed tumors, and for inspection of the corresponding lung for metastases and for the status of the opposite kidney. His technique involves an approach through the bed of the eighth rib.

RIGHT THORACOABDOMINAL INCISIONS

In 1949 Devine and Burwell[6] had the opportunity to utilize a right thoracoabdominal incision introduced to Devine by John M. Chamberlain during World War II. While operating through a right rectus incision on a patient who had sustained an injury to the abdomen, a laceration about 5 cm. in diameter was seen in the right lobe of the liver at the superior end of the abdominal wound. The incision was then extended into the chest between the fifth and sixth ribs, which, after section of the diaphragm, easily exposed the lacerated area (Fig. 3, *A*). The patient made an uneventful recovery.

Heaney and Humphreys,[12] realizing the need for a right thoracoabdominal incision in procedures confined to the right upper quadrant, devised a procedure which removes the barrier of the right costal margin. This type of incision would be especially applicable in very obese patients. With this type of incision, the right lobe of the liver may be rotated into the chest, thereby exposing the right upper quadrant structures more readily. They first used their incision in the anatomic laboratory and, after establishing a technique, employed it on dogs and in the post-mortem room. They have reported its use on one extremely obese patient on whom a simple cholecystectomy was performed in order to test its worth. I quote their description of the technique:

> A long curved incision is made overlying the ninth intercostal space. It is extended from the mid-axillary line downward and forward across the costal margin, and over the abdomen to the linea alba five centimeters above the umbilicus (Fig. 3, *B*). This incision is carried through the subcutaneous tissue to expose the external oblique muscle and the anterior rectus sheath. The latter is divided transversely as is the right rectus muscle. The external oblique muscle is split in the direction of its fibers, whereas the internal and transversus abdominis are divided in the line of the incision. The common costal cartilage is divided between the ninth and tenth ribs and the chest is entered through the ninth interspace. The abdomen is then entered by means of a radial incision through the diaphragm which extends from its periphery at the point of division of the costal cartilage to the right dome. Following this, the peritoneum

is divided throughout the abdominal segment of the wound. A Finochietto retractor is placed between the ninth and tenth ribs and spread. In this manner the wound is held wide open without other retraction. Next, the right lobe of the liver is gently rotated upward through the diaphragmatic defect into the right lower chest, exposing the gall bladder, the porta hepatis, the gastro-hepatic omentum, the vena cava, and the pancreaticoduodenal region admirably, in spite of the patient's great obesity.

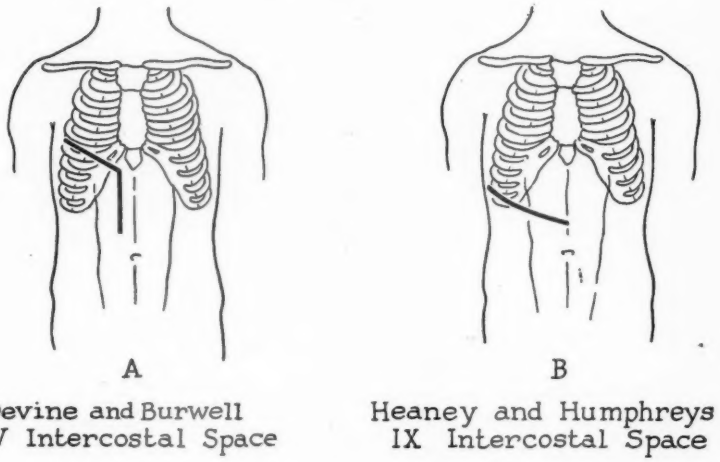

Fig. 3.—Right thoracoabdominal incisions.

The cholecystectomy progressed without incident and the postoperative course was marred only by a transient right lower lobe atelectasis. The authors stated that an easier closure might be effected if the rib was resected, especially in the very obese patient. They believed that the right thoracoabdominal approach was useful in (1) secondary and tertiary operations upon the biliary tract when landmarks have been obliterated by adhesions from previous procedures, (2) plastic procedures on the bile ducts, (3) operations upon the pancreaticoduodenal area, (4) exposure of the portal vein and inferior vena cava for the performance of an Eck fistula (Blakemore uses this incision for such a procedure), (5) removal of the right lobe of the liver, as the inferior vena cava is easily exposed above and below the liver, (6) removal of upper right quadrant structures through the chest alone, especially in those individuals with an exceptionally high diaphragm, (7) neoplastic lesions involving the right lobe of the liver and the right lower lung field, and (8) an extension of the usual right upper quadrant incision when difficulty of exposure is encountered.

COMMENT

It is apparent that the thoracoabdominal incision has a definite place in the armamentarium of the general surgeon. Regardless of the choice of the surgeon of a vertical or transverse abdominal incision, there are means of extending that incision for a wider exposure of the upper abdominal viscera, both right and left. Whether one employs the intercostal space or rib technique is unimportant, though it may be wiser to employ the rib resection tech-

TABLE I. HISTORICAL DEVELOPMENT OF THE THORACOABDOMINAL INCISION

AUTHOR	YEAR	
Lannelongue	1895	Described an extrapleural osteochondral flap procedure, never employed on a living subject.
Micheli	1895	Described an extrapleural flap approach never employed on a living subject.
von Mikulicz	1896	Resected a carcinoma of the lower esophagus utilizing an extrapleural osteochondral flap approach.
Marwedel	1903	Resected a stenosis of the lower esophagus through a costal margin release procedure.
Sauerbruck	1905	Advocated two incisions, a laparotomy and a thoracotomy. He never employed the procedure.
Tiegel (Henle)	1909	Resected a carcinoma of the cardia through two incisions; utilized a Murphy button for the anastomosis.
Wendel	1909	Employed a two-incision technique, resulting in an esophagostomy and a gastrostomy, for carcinoma of the lower esophagus.
Janeway and Green	1910	Employed a two incision technique with resection of the lesion, carcinoma of the lower esophagus, through the chest. First suggestion of a one incision technique.
Zaaijer	1911	Employed primary thoracoplasty and gastrostomy followed by a one-incision technique.
Kirschner	1920	Employed a one-incision technique through the seventh intercostal space.
Hedblom	1922	Employed a similar two-stage technique patterned after Zaaijer.
Ohsawa	1933	Reported the first series of cases utilizing two approaches, Marwedel's costal release and the procedure suggested by Janeway and Green.
Garlock	1941	Employed a two-incision approach, primary abdominal inspection followed by resection through the chest.
Brock	1942	Reported the first successful esophagogastrostomy from Europe. Employed a single incision technique through the sixth intercostal space.
Wu and Loucks	1942	Reported seven cases of carcinoma of the lower esophagus and the cardia resected through a single incision in the bed of the seventh rib.
Garlock	1946	Employed a primary abdominal exploration with extension of the incision through the eighth intercostal space.
Humphreys	1946	Employed a single incision with extension through the eighth intercostal space.
Harper	1947	Employed primarily a thoracotomy through the ninth rib bed with a short abdominal extension.
Kremen	1948	Employed a primary abdominal incision with extension through the seventh intercostal space.
Campbell, Alexander, and Mikal	1949	Employed a vertical abdominal incision with extension through the seventh or eighth rib bed.
Carter Carter and Helmsworth	1947 1950	Employed a transverse abdominal incision with extension into the eighth intercostal space, occasionally the seventh space.
Wangensteen	1951	Employed a midline upper abdominal incision with a sternotomy into the fourth intercostal space.
Longmire	1952	Employed a diagonal incision over the costal margin with transection of the costal margin and the ends of the sixth, seventh, and eighth ribs, thereby forming a costal margin extrapleural flap much like Marwedel.

nique in the older age group. The Wangensteen extrapleural technique certainly is an innovation in abdominal incisions. Only experience will determine its value. The routine employment of closed drainage of the chest for the first forty-eight hours or more postoperatively cannot be overstressed. The careful closure of the diaphragm with interrupted sutures and the approximation of the costal margin with steel wire will help prevent further complications after the thoracoabdominal approach.

CONCLUSIONS

1. The historical development of thoracoabdominal incisions has been presented.

2. The various techniques in use today have been described in detail.

3. The employment of the combined incision in certain types of lesions has been briefly discussed.

4. Suggestions have been presented in order to avoid postoperative complications.

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Surgical Technique

A COMPARISON OF THE DUPLAY AND DENIS BROWNE TECHNIQUES FOR HYPOSPADIAS OPERATIONS

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IN THE June, 1952, issue of the JOURNAL my operation for hypospadias was criticized at length by Dr. Donald R. Smith and Dr. Harry M. Blackfield.[4] They had two objections. The first is that "it appears to violate some fundamental principle of surgery" and that "it is doubtful whether it will stand the test of time." The second is that it is "resurrected in all its aspects" from an operation first reported over seventy years ago by Duplay[1] and described at length in the writings of a well-known contemporary French surgeon, Marion.[2] This appears to mean that the operation is a rash and unproved proceeding, and at the same time simply the oldest, and probably the best known, of all classical procedures for hypospadias.

The first suggestion that my operation was identical with that of Duplay was made by Nesbit, Butler, and Whittaker in 1950,[3] in an account of experimental burying of strips of fur-bearing skin animals. I regarded this suggestion as an oddity that would not survive the comparison of their own figures of my operation with those of the operation of Duplay, although his original papers are far from easy to obtain. In this I was wrong.

Bickerings about small points of surgical originality are not to be encouraged, but these statements show such a misunderstanding of what I think will probably prove a very useful procedure that examination of them may be of general interest.

Now in assessing an operation it is of advantage (a) to have seen it performed by a competent surgeon, if not to have performed it oneself; (b) to have inspected both late and early results (in the case of operations for hypospadias urethroscopy is essential for this); (c) to consider opinions published by reputable surgeons who have used it; and (d) to read the published accounts with great care and, in the case of those in a foreign language, to make sure that the wording is understood.

Investigation of the operations under discussion by those observing these conditions will reveal certain points of difference between them.

1. Before the working out of my technique every surgeon, without exception as far as I know, constructed at the time of operation some kind of tube, complete or incomplete, to form the new urethra. In Duplay's first published technique (1874) a complete tube was constructed around a cathe-

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ter and he noted that it did not really matter if the edges of this tube could not be brought together everywhere. In a later paper of 1880[1] he took this observation a stage further, and remarked "although the catheter is not really covered, I have been able to convince myself that there are no ill effects upon the new canal." Apparently he was not able to convince anyone else, not even Marion, who constructed a complete tube, although not with a separate line of sutures. This is obvious to anyone who reads Marion's works and studies his illustrations; his tension suture runs under the raw surface to within 1 mm. of the edge of the central skin strip, and if investigation is carried to the length of experimenting with such a stitch it will be found that the results are exactly as shown in Fig. 528 of Marion's *Traité d'urologie*.[2] (Admittedly this shows the treatment of a large fistula, but the stitch and the phrase used to describe it are exactly the same as those used in the construction of the urethra.)

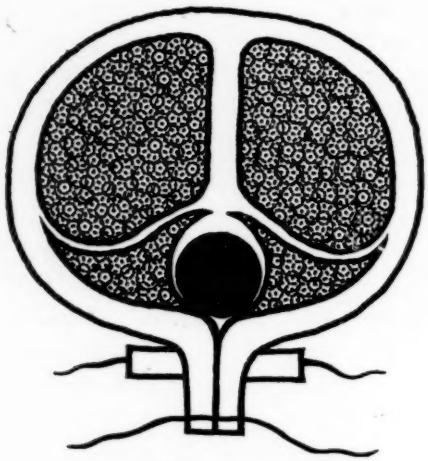

Fig. 1.

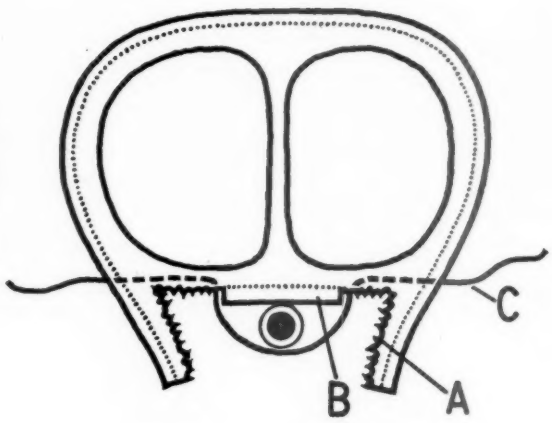

Fig. 2.

Fig. 1.—Exact copy of Duplay's original illustration of his operation to show the forming of a tube of penile epithelium around a catheter.

Fig. 2.—Diagram of the insertion of a stitch in Duplay's operation, as described by Marion. *A*, Raw surface of lateral flap; *B*, strip of skin which the stitch will wrap around the catheter when tightened; and *C*, stitch.

From Duplay's teaching, that it does not matter if a tube is incompletely formed, to my own, that it is a mistake to try to make a tube at all, there is a considerable step and, as far as I know, I am the first who made it. The lack of any development of Duplay's interesting suggestion is probably due first to the apologetic way in which he put forward an idea which was (as I am constantly told about my own) contrary to the principles of surgery, and second to the very unconvincing evidence he offered of its success. One must give him all credit as a pioneer attacking an unsolved problem under difficulties which require an effort of the imagination to realize today but, all the same, of his five recorded cases only two had a "happy result" without an unspecified number of secondary operations to complete the second stage, with a third difficult one to come. Those who worked out the "percentages of fistula formation" must have hardly felt encouraged to proceed further on the same lines.

In my operation, the essential idea is to leave the buried skin as a flat untouched strip, from which epithelium, indistinguishable from ordinary penile skin, will grow around the joining raw surfaces of the lateral flaps until it meets in the midline.

The advantages of this are:

a. The final circumference of the epithelial-lined tube is considerably bigger than the original breadth of the buried strip. It is difficult to be sure how much bigger it is, but it is probably between 30 and 60 per cent. Those who do not believe this should try urethroscoping in cases where the strip has settled down.

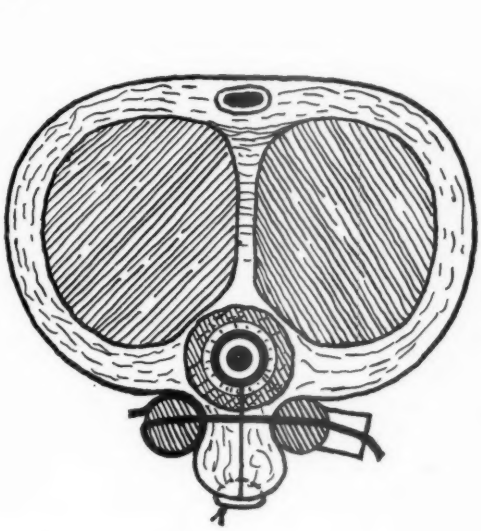

Fig. 3.

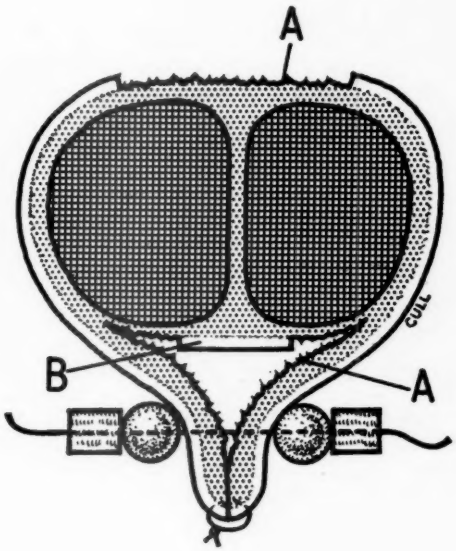

Fig. 4.

Fig. 3.—Exact copy of Marion's illustration of the result of the stitch shown in Fig. 2.

Fig. 4.—Diagram of the Denis Browne operation in contrast with Figs. 1 and 3, showing a flat untouched strip of skin buried deeply under raw surfaces. Note that the double-stop sutures do not quite join the raw surfaces, and ac tsimply as tension sutures.

A, Raw surface of lateral flap and dorsal incision; and *B*, buried strip of untouched penile skin.

b. There is always a free way of escape for urine, pus, blood, or serous discharge. One of the weak points of such methods as Edmunds', which like my own included construction of the new urethra in continuity with the old, was that the distal tube was often so blocked by swelling or discharge that it was burst open as fluid attempted to escape.

If I have borrowed this idea, it is from the operation for excision of strictures evolved by that still insufficiently appreciated surgeon, Hamilton Russell. It is curious that with all his interest in hypospadias he did not see that he had the solution of the problem under his hand.

2. The incisions for the two operations are entirely different, as will be seen from Figs. 5 and 6. It will be found interesting to attempt to sketch in on photographs of the severer varieties of the deformity the incisions recommended by various authors; in the great majority of them this cannot be done.

3. One of the main points of my technique is the inclusion of a wide separation between the buried strip and the outer skin, so that it is difficult for epithelium to shoot across from one surface to the other and so form a fistula. In the Duplay operation both surfaces are left to heal close together. It is a lack of understanding of this point which accounts for the remark that it is difficult to say why my technique should be so free from fistula formation.

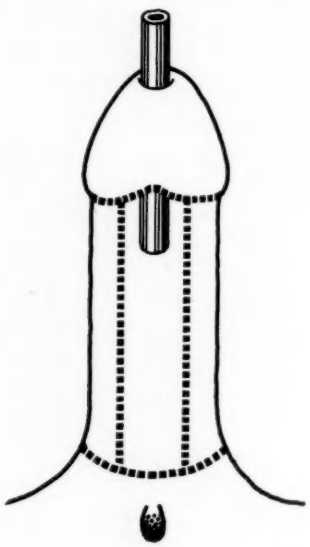

Fig. 5.

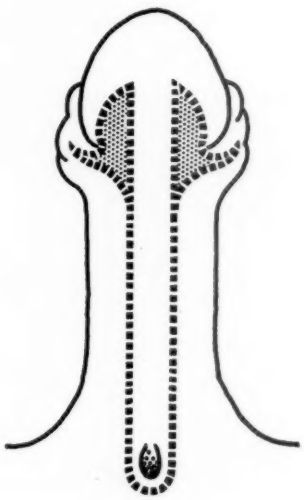

Fig. 6.

Fig. 5.—Illustration showing the incisions for Duplay's operation, diagrammatically rendered from his original illustration.

Fig. 6.—Incisions on ventral surface of penis for Denis Browne illustration. Contrast with Fig. 5.

4. The Duplay technique forms a new urethra around a catheter. I consider the catheter unnecessary, an encouragement to sepsis, and an obstacle to circulation.

5. The Duplay technique forms the new urethra as a separate tube, and it requires a final and far from easy operation to connect this to the original opening. I form the new tube in continuity with the original short urethra, in one stage.

6. The Duplay technique does not use a dorsal incision. This is an essential part of my technique for four reasons.

(a) It does away with all tension on the joining edges.

(b) It allows expansion in an erection.

(c) Owing to the exudation from the raw area, there is much less edema than would otherwise occur in the few days after operation, and edema is the greatest of all hindrances to complete and rapid healing.

(d) It distributes the reservoir of penile skin in the prepuce to where it is needed, the undersurface and base of the penis. Duplay's operation ignores the preputial skin altogether. I originally had a number of hard-won successes using the technique of Edmunds, which by way of complicated and

difficult steps splits the prepuce dorsally and swings it around as two flaps to cover the new urethra. Then it occurred to me that the simple solution of my difficulties was to rely upon the extreme mobility and extensibility of the penile skin, and to allow it to adjust itself to the stresses put upon it once it was freed by a full-length dorsal incision. It is particularly in this respect that it is advantageous to see the operation performed before deciding whether it will work.

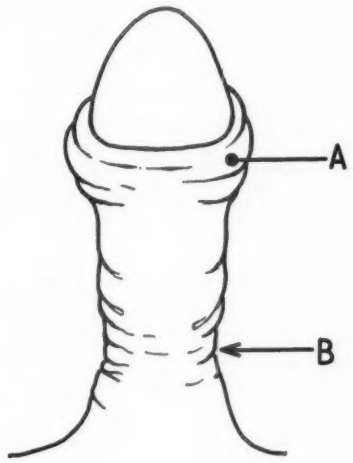

Fig. 7.

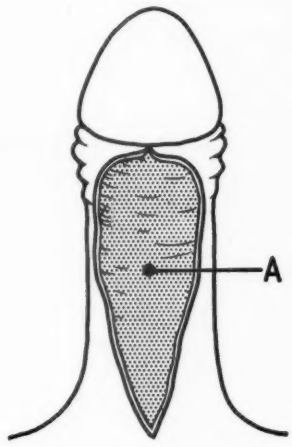

Fig. 8.

Fig. 7.—Dorsum of penis after Duplay's operation. *A*, Prepuce, still in condition much like its original state before operation; and *B*, zone of great tension in an erection, inevitably produced by this operation.

Fig. 8.—Dorsum of penis in Denis Browne's operation. *A*, Raw surface left by dorsal incision. Note that prepuce has almost disappeared because of pulling of its skin onto the ventral surface.

Duplay made some rather vague remarks about originally having used a dorsal incision in some cases, but he classed this as an inconvenience which his later technique enabled him to avoid. Marion does not use it at all.

I may say here that it is obvious to anyone who analyzes my operation that its debt to Edmunds is far greater than its debt to Duplay. Two of Edmunds' teachings survive in it, the making of the new urethra in continuity with the old, and the use of the preputial skin in covering it over. I think this covering of the penis with penile skin is essential for an ideal result. At one time I experimented with a technique differing only in details from that of Smith and Blackfield but gave it up for the reason, among others, that I thought that a penis whose underside was covered with hairy scrotal skin would worry a good many people of both sexes.

7. The Duplay technique involves a tunnel through the glans. I consider this an addition to the dangers and difficulties of the operation without any counterbalancing advantages. One surgeon has endeavored to improve my technique by cutting into the glans, with disastrous results. Marion has given up the glandular tunnel.

8. The Duplay technique includes the use of stitches piercing a length of catheter to join the lateral flaps. This continuous bar has the obvious fault

of interfering with free circulation to the healing edges, while the separated points of pressure of my double-stop sutures do not.

The ancient device of using lead shot to hold a suture has two disadvantages. (a) The shot is deformed by crushing it, so that it meets the skin in an irregular and often sharp-pointed shape. (b) Lead is too soft for this purpose; a suture can always be pulled through it.

My double-stop technique of using a bead for the function of pressing on the skin (in other operations, such as abdominal sections, buttons of suitable size may be substituted for the bead) and an aluminum cylinder for the separate function of gripping the suture avoids both these troubles.

9. It is a really important point of difference that whereas Duplay and Marion use the stopped sutures for the actual joining of the raw surfaces I use them to combat tension alone. If they are pulled tight enough to jam together (*adosser*) the healing surfaces of the flaps, there is the risk of a fistula through a stitch hole. Thus, whereas Duplay uses fine stitches on the skin edges only when these tend to gape, I rely upon these stitches entirely for the actual joining of the skin. Once this skin has joined, the tension sutures are taken out and the skin is allowed to slip dorsally and narrow the gap remaining there.

10. Duplay depends upon a urethral catheter for keeping urine out of the wound in the final stages of his operation. I have found that leakage is likely to occur despite this. Marion drains the bladder suprapubically throughout the progress of the series of operations. The suffering to the parents and child and the worry to the surgeon of months of suprapubic drainage are avoided by the ten days of perineal drainage which I recommend. The small puncture in the urethra closes a few days after removal of the tube. In addition, suprapubic drainage is quite ineffective in keeping urine out of the urethra, as I have explained elsewhere.

11. Duplay's operation is not well suited to either the slightest or the severest degree of the deformity, which my technique handles with ease and with at least one less operation than his requires.

The various types in succession are:

a. Stenosis of the meatus in glandular hypospadias: In many cases the displacement of the meatus is so slight as not to affect either appearance or function, but in most of them the meatus is unduly small. There is invariably a minute blind sinus distal to the meatus in such cases, and by putting one blade of a very fine blunt-pointed scissors into this, and the other blade into the urethra, it is possible to connect the two openings by cutting through the tissues between them. In this way the meatus is enlarged without shortening the already short tube.

b. The subglandular opening: Merely an attempt at drawing the operation will show the difficulty of applying either the Duplay or the Marion technique to this.

c. The perineal opening: The operations of Edmunds, Ombrédanne, McIndoe, and Smith and Blackfield abruptly cease to be workable once the open-

ing appears behind the scrotum. It will have been noticed after a study of the literature of the subject that these openings are vaguely mentioned and not illustrated in accounts of operations. Duplay's method would, with considerable difficulty of application, work here, but the final stage would be the closing of a fistula of the perineum.

My own technique handles such openings without any difficulty at all; the remark of Smith and Blackfield that skin grafting would be necessary to avoid a hairy inner lining to the urethra shows their failure to notice that in all such cases there is a groove lined with mucosa leading forward from the opening (Fig. 11). (I also disagree with their statement that the corpus spongiosum is present in hypospadias. My experience confirms the opinion of all other authorities I have read who agree that where there is no urethra there is none of the erectile tissue that normally surrounds it.)

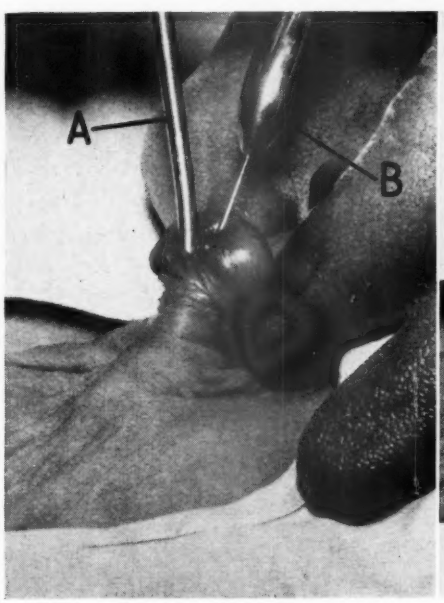

Fig. 9.

Fig. 10.

Fig. 9.—Photograph of a glandular hypospadias showing *A*, a catheter introduced into the urethral opening, and *B*, a fine probe introduced into the blind sinus that invariably exists distal to urethral openings in this position.

Fig. 10.—Denis Browne's meatotomy for such cases as are shown in Fig. 6. One blade of the fine blunt-pointed scissors is thrust into the opening of the urethra, and the other into the opening of the blind sinus. When closed they connect the two passages and so enlarge the narrow meatus.

d. Intersex cases with a rudimentary vagina behind the urethral opening: Many of these persons are brought up as males, and it is essential for their happiness that they be able to urinate standing up. In several such cases I have covered in the small vagina as part of the new urethra, with or without removing the rudimentary uterus above, and there have been no ill effects. I think it is advisable to drain the vagina separately by an additional fine tube, to avoid the accumulation of urine which may have leaked around the bladder catheter.

e. A buried ectopic urethral anus combined with hypospadias: The buried anus is exposed by slitting the urethra, and it is dilated until it works normally. This leaves the urethral opening on the very edge of the anus. In my two cases of this condition, the new urethra has been constructed from there to the end of the penis in one simple operation. It was, of course, necessary to drain the bladder through the wound itself, but I found no difficulty in this.

12. Marion recommends waiting five or six years before constructing the new urethra. Duplay left the final stage until the "age of reason" which he very reasonably did not define. We perform the first stage at eighteen months, and consistently send our patients off to school at the age of 5 years passing urine in the upright position like other boys. This is far from unimportant to the sensitive developing boy.

Fig. 11.—Photograph of perineal hypospadias, showing the groove lined with mucosa that invariably exists in such cases in front of the abnormal opening.

I think that consideration of these points will cause doubt as to whether the assertion that the Duplay operation and mine are identical can be made by anyone who understands any of the techniques involved. The final stage of confusion on this point was reached when Smith and Blackfield, having said that Duplay's operation is the same as mine, and that mine is inadvisable, then proceeded to advise what they call a Duplay urethroplasty. This proceeding involves construction of a complete tube (as I do not) in continuity with the abnormal urethra (as Duplay did not).

The criticism that my operation "seems to violate some fundamental principle of surgery" would be easier to answer if the principle were defined. However, I accept it as the usual tribute of the profession to a new idea. I suggest that a fundamental principle of surgery is to realize that different structures behave in different ways and to treat them accordingly. Peri-

toneum does not behave like pleura, and still less like dura mater. Similarly, penile skin does not behave like abdominal skin, and still less like the coat of a dog or rabbit; in many ways it behaves like mucosa, from which it can develop, as has been shown by the results of circumcision. Now, mucosa will heal over a raw surface far more rapidly and efficiently than ordinary body skin and it does not form keloid; penile skin behaves in much the same way. Consider the fistulas that used to plague us; they are lined with skin indistinguishable from the original covering of the penis, and they have no tendency to contract; a fistula that will barely admit a bristle will persist in exactly the same condition for years. In consequence, the principle behind my operation, that of leaving penile skin or mucosa to cover spontaneously a raw surface, has many applications, some of which I list here.

a. The closing of fistulas of the urethra, whatever their position or origin: This becomes easy and certain if the tube itself is not sutured but allowed simply to fall away from the outer skin, which is then closed by double-stop sutures.

b. The fashioning of a urthera in epispadias: Here the mucosa forming the bottom of the dorsal groove in the glans is simply buried, after enough of its invariably excessive amount has been removed to leave two broad areas of raw surface on either side. If any further evidence is needed that Duplay and Marion did not have the idea of simple burial of a strip, it can be found in their treatment of epispadias.

c. The fashioning of a working bladder sphincter in epispadias with incontinence: I have had a number of successes in this difficult condition by denuding the neck of the bladder of all mucosa except a narrow strip and then suturing the muscle tightly around this. The approach, for which no originality is claimed, has been made by dividing the symphysis pubis in the male patient, and it is essential to make a longish tube in this manner.

d. Urethral strictures: Although it is not my own work, I may mention a most promising combination of my hypospadias technique with Hamilton Russell's orginal operation for excision of urethral strictures worked out by some Scandinavian surgeons, in particular Dr. Bengt Johanson of Stockholm. This consists in slitting up the stenosed urethra, excising the scar tissue, and so allowing a sort of groove to form in the perineum, lined with mucosa or new skin. When all has epithelized, this groove is covered in, and forms a new wide-bore urethra.

As I am writing this I have just seen a similar application of this principle described by Swinney.[5]

e. Fashioning a new lacrimal duct by simply pulling a strip of mucosa through from conjunctiva to nose.

f. Forming the labiogingival groove in cases of double harelip with displaced premaxilla: One of the many requirements of a successful result in these cases is a sulcus of normal dimensions between the joined lip and gum. If the lip is held separate from the underlying bone in the first stage of the operation, both surfaces heal over with mucosa, and so avoid a long, difficult, and often disappointing piece of skin-grafting at a later stage. I would suggest that in

the cases where this groove has not been procured early, much better results will be gained by simply separating the lip from the bone by a plastic plate and allowing mucosa to cover the raw surfaces than would be obtained by the usual procedure of applying a split skin-graft.

g. Freeing the ends of the gap in the nasopharyngeal sphincter in cleft palate operations: I believe that to make an orthopedic job of this, that is to get the actual ends of muscle together and leave the sphincter closed during healing, it is necessary to do far more drastic freeing than has ever, to my knowledge, been done before. The huge gaps that I leave by detaching the soft palate from the tongue fill in with surprising rapidity and epithelize with very little contraction.

Concerning results, as I have stated, I began operating following the methods of Edmunds, who had, I was convinced, the right fundamental ideas. At that time there was a large and melancholy class of these patients attending The Hospital for Sick Children, coming up time after time for proceedings that at best took several stages, and that nearly always needed a series of secondary operations. I even published one of many variations I worked out; the only value of this paper now is its mention of a method of meatotomy, described earlier, which we now very frequently use in the common cases of glandular deformities. Then, suddenly, all the pieces of the puzzle fell into place, and within a year the waiting list was wiped off and the operation became a routine one like that for inguinal hernia. When I first described it at a meeting of the Royal Society of Medicine it was greeted with complete disbelief by all specialists in plastic surgery, but was so rapidly adopted in many quarters that I published it in rather a hurry, not wishing to see it come out under another name. It is worth remarking that although it has been widely taken up on the continent of Europe, no one there has suggested that it is Duplay's operation, perhaps because the French language is widely understood.

The real test of a technique is not what the originator says he can do with it, but what other surgeons find when they try it. Two standard works on the urology of childhood, those of Campbell[12] and Higgins, Williams, and Nash,[11] quote my operation as the most satisfactory the authors have tried. I need hardly refer to the generous and able expositions of my technique that have been made by Burns,[13] in the United States, and Dr. Bengt Johanson informs me that he will very shortly publish an account of his first 100 cases in which my technique was used, together with urethroscopic reports.

The results to date at The Hospital for Sick Children are seen in Table I. The operations have been performed by ten different surgeons, of varying experience and skill.

TABLE I

TYPE OF OPERATION	NUMBER	FISTULAS
Perineal	14	4
Midscrotal	17	2
Penoscrotal	32	1
Midshaft	50	1
Subcoronal	21	0
Total	134	8

Six of these patients had had multiple previous attempts at repair. No patient had more than one fistula, and all fistulas were closed in a single operation. The high percentage of fistulas in the perineal cases (which include those of hermaphrodites and intersex) did not occur in the perineal region, but was due to the extremely minute size of the penis in many of the patients. There have been no strictures, and urethroscopy has shown, on all those examined, the wide-bore urethra I have described. I am of the opinion that several of these patients could have been managed by no other technique.

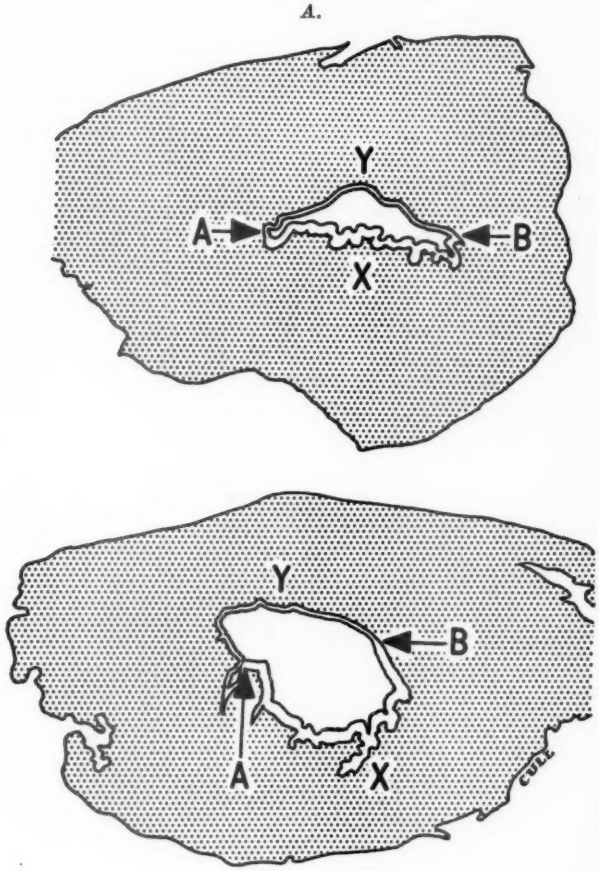

Fig. 12.—Tracings of photomicrographs by Dr. Bengt Johanson. *A*, A buried strip of penile mucosa two years after operation. *AXB*, Original mucosa; and *AYB*, new epithelium. *B*, A buried strip of penile skin two years after operation. *AXB*, Original skin; and *AYB*, new epithelium.

ADDENDUM

Since this paper was submitted, Dr. Bengt Johanson[15] has published the work referred to in it. It includes: (1) a follow-up of my first fifty cases, all with satisfactory results. Only two fistulas occurred, which were both closed by the time of examination. Two cases could not be traced. (2) a series of experiments on the penes of dogs, which show that, if either penile skin or urethral mucosa is buried in the way I have described, new noncontractile lining is formed so that the resulting tube has a circumference nearly double that of the width of the original strip (Fig. 12). The new lining has the same characteristics whether it starts from skin or mucosa.

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Book Reviews

Books Received

The receipt of books is acknowledged in this section and this treatment must be regarded as sufficient acknowledgment of the courtesy of the senders. Selections will be made for more extensive review dictated by the interests of our readers as space permits.

PROSTATECTOMY—A METHOD AND ITS MANAGEMENT. By Dr. Charles Wells, Professor of Surgery, University of Liverpool. Price $5. Pp. 103, with 72 illustrations. Edinburgh and London, E. & S. Livingstone.

MANUAL OF GYNECOLOGY. By E. Stewart Taylor, M.D., Professor and Head of Department of Obstetrics and Gynecology, University of Colorado School of Medicine, Denver. Pp. 204, with 70 illustrations. Philadelphia, Lea & Febiger.

1952 YEAR BOOK OF GENERAL SURGERY. By Evarts A. Graham, M.D., Emeritus Professor of Surgery, Washington University School of Medicine, and Stuart C. Cullen, M.D., Professor and Chairman of Division of Anesthesiology, State University of Iowa College of Medicine. Price $6. Pp. 670, with 203 illustrations. Chicago, The Year Book Publishers, Inc.

ANZEIGE UND AUSFÜHRUNG DER EINGRIFFE AN OHR, NOSE UND HALS. By Walther Uffenorde, M.D., Hellmut Uffenorde, M.D., and Horst Wullstein, M.D. Price DM 79.80. Pp. 540, with 408 illustrations. New York, Grune & Stratton, Inc.

DAS INSELSYSTEM DES PANKREAS. By Prof. Dr. H. Ferner, Hamburg, Germany. Price DM 29.70. Pp. 186, with 54 illustrations. Germany, Georg Thieme Verlag, Agent for U. S. A.: Grune & Stratton, Inc., New York, N. Y.

DIE ANGIOGRAPHIE ZUR ERKENNUNG, BEHANDLUNG UND BEGUTACHTUNG PERIPHERER DURCHBLUTUNGSSTÖRUNGEN. By Dr. Habil H. W. Passler, Leverkusen, Germ. Price DM 26.70. Pp. 115, with 102 illustrations. Germany, Georg Thieme Verlag, Agent for U. S. A.: Grune & Stratton, Inc., New York, N. Y.

SURGERY FOR NURSES. By James Moroney, M.B., Ch.B., F.R.C.S., L.R.C.P., London. Price $6. Pp. 676, with 585 illustrations. Edinburgh and London, E. & S. Livingstone.

OPERATING ROOM TECHNIC. St. Mary's Hospital, Rochester, Minn. Pp. 345, with 219 illustrations. Philadelphia, W. B. Saunders Company.

GRUNDRISS DER ELEKTROKYMOGRAPHIC. By Dr. K. Heckmann, Muchen, Germ. Price DM 6.60. Pp. 36, with 5 illustrations. Germany, Grune & Stratton, Inc.

PRINCIPLES OF NEUROLOGICAL SURGERY. By Dr. Loyal Davis, Chairman of Division of Surgery, Northwestern University Medical School. Price $8.50. Pp. 554, with 354 illustrations. Philadelphia, Lea & Febiger.

1953—MEDICAL PROGRESS. By Dr. Morris Fishbein. Price $5. Pp. 301. Garden City, N. Y., The Blakiston Company.

STEPHANIA. By Ilona Karmel. Price $3.75. Pp. 375. Cambridge, Mass., The Riverside Press, Houghton Mifflin Company.

LA CHIRUGIE DU REIN EN FER A CHEVAL. By P. Macquet and L. Wemeau, Clinique Urologique, Universitaire de Lille. Pp. 99, with 19 illustrations. Paris, Masson & Cie.

PLASTIC SURGERY AT THE NEW YORK HOSPITAL 100 YEARS AGO. By Herbert Conway, M.D., and Richard B. Stark, M.D. Price $5. Pp. 110, with 29 illustrations. New York, Paul B. Hoeber, Inc.

DAS ULKUS DES MAGENS UND ZWÖLFFINGERDORMS. By Dr. H. Ramb, Chefarzt der Chirurg, Abteilung am Laurentuis-Hospital Essen-Sterle. Price DM 6.50. Pp. 68, with 28 illustrations. Stuttgart, Germ., Georg Thieme Verlag, Agent for U. S. A.: Grune & Stratton, Inc., New York, N. Y.

OPHTHALMIC SURGERY. By Dr. J. Meller, revised by Prof. Dr. J. Bock, University of Gratz, Austria. Price $12. Pp. 529, with 283 illustrations. Garden City, New York, The Blakiston Company.

TECHNIK DER BLUTGRUPPEN UND BLUTFAKTOREN BESTIMMUNG. By Dr. Med. Habil Peter Dahr, University Gottingen, Germ. Price DM 24.00. Pp. 320, with 27 illustrations. Stuttgart, Germ., Georg Thieme Verlag, Agent for U. S. A.: Grune & Stratton, Inc., New York, N. Y.

DIE GESUNDE UND DIE KRANKE WIRBELSAULE IN RÖNTGENBILD UND KLINIK. By Dr. Georg Schmorl, Prof. Dr. Herbert Junghanns, Oldenburg, Germ. Price DM 72.00. Pp. 304, with 403 illustrations. Stuttgart, Germ., Georg Thieme Verlag, Agent for U. S. A.: Grune & Stratton, Inc., New York, N. Y.

DIE KONSERVIERUNG DES KNOCHENGEWEBE FÜR TRANSPLANTATIONEN. By Dr. Hans Roth, Vienna. Price $11.60. Pp. 222, with 147 illustrations. Vienna, Austria, Springer-Verlag.

ENCYCLOPEDIA OF ABERRATIONS. By Dr. Edward Podolsky, State University of New York Medical College. Price $10.00. Pp. 550. New York, Philosophical Library, Inc.

SYNOVIAL FLUID CHANGES IN JOINT DISEASES. By Dr. Marion W. Ropes and Dr. Walter Bauer, Massachusetts General Hospital, Boston. Price $4. Pp. 150, with 15 illustrations. Cambridge, Mass., Harvard University Press.

OPERATIVE GENECOLOGY. By Richard W. Te Linde, M.D., Johns Hopkins University and Hospital, Baltimore. Price $20. Pp. 902, with 409 illustrations. Philadelphia, J. B. Lippincott Company.

PHYSIOLOGICAL FOUNDATIONS OF NEUROLOGY AND PSYCHIATRY. By Dr. Ernst Gelhorn, Professor of Neurophysiology, University of Minnesota. Price $8.50. Pp. 556, with 107 illustrations. Minneapolis, University of Minnesota Press.

FUNCTIONAL AND SURGICAL ANATOMY OF THE HAND. By Dr. Emanuel B. Kaplan, College of Physicians and Surgeons, Columbia University, New York. Price $16. Pp. 288, with 132 illustrations. New York, J. B. Lippincott Company.

HUMAN ANATOMY. By Dr. J. Parsons Schaeffer, Professor of Anatomy, Jefferson Medical College. Price $16. Pp. 1,718, with 1,220 illustrations. New York, The Blakiston Company.

DIE LUNGENRESEKTIONEW. By Prof. Dr. A. Lezius, Hamburg. Price DM 49.80. Pp. 143, with 112 illustrations. Stuttgart, Germ., Georg Theime Verlag, Agent for U. S. A.: Grune & Stratton, Inc., New York, N. Y.

THE PHYSICIAN IN ATOMIC DEFENSE. By Dr. Thad P. Sears, University of Colorado School of Medicine, Denver. Price $6. Pp. 308, with 53 illustrations. Chicago, The Year Book Publishers, Inc.

WIEDERHERSTELLUNGSCHIRURGIE UND TRAUMATOLOGIE. RECONSTRUCTION SURGERY AND TRAUMATOLOGY. CHIRURGIE REUARATRICE ET TRAUMATOLOGIE. By M. Lange, Bad Tölz, Oberbayern, Germ. Price Swiss francs 36.00. Pp. 262. Basel, Switzerland, S. Karger.

LO ESENCIAL EN ORTOPEDIA. By Philip Wiles, M.S., F.R.C.S., F.A.C.S., London. Pp. 496, with 365 illustrations. Buenos Aires, Argentina, de la Escurela Finochietto.

CONDUCTION ANESTHESIA. By Dr. George P. Citkin, F.A.C.S., F.I.C.S. Price $22.50. Pp. 1,005, with 585 illustrations. Philadelphia, J. B. Lippincott Company.

TUMORS OF BONE. By Dr. Bradley L. Coley and Dr. Norman L. Higinbotham, Cornell University Medical College, New York. Price $10. Pp. 216, with 172 illustrations. New York, Paul B. Hoeber, Inc.

CLINICAL ORTHOPOEDICS. By Anthony F. DePalma, M.D., Philadelphia. Price $6. Pp. 242, with 149 illustrations. Philadelphia, J. B. Lippincott Company.

ANNUAL REVIEW OF MEDICINE. By Dr. Windsor C. Cutting, Dr. Henry W. Newman, Associate Editor, Stanford University School of Medicine. Price $6. Pp. 452. Stanford, Calif., Goerge Banta Publishing Company.

SHOULDER LESIONS. By Dr. H. F. Mosely, Montreal, Canada. Price $12. Pp. 329, with 216 illustrations. New York, Paul B. Hoeber, Inc.

BLOCKADE UND CHIRURGIE DES SYMPATHICUS. By Dr. Felix Mandl, Vienna. Price $12.40. Pp. 388. Vienna, Austria, Springer-Verlag.

GINGIVITIS IN MILITARY PERSONNEL WITH SPECIAL REFERENCE TO ULCEROMEMBRANOUS GINGIVITIS. By Dr. J. J. Pindborg, Copenhagen. Pp. 93. Copenhagen, C. A. Reitzel.

RÖNTGENUROSKOPIE NIERENBECKEN UND KELCHE HARNLEITER, BLASE, HARNRÖHRE. By Dr. Habil. G. W. Gunther, Mannheim, Germany. Price DM 13.50. Pp. 43, with 85 illustrations. Mannheim, Germ., G. W. Gunther.

1953 NEW AND NONOFFICIAL REMEDIES. Council on Pharmacy and Chemistry, American Medical Association. Pp. 623. Philadelphia, J. B. Lippincott Company.

CIRUGIA DEL ESOFAGO Y HERNIAS DEAFRAGMATICAS. By Dr. Alfonso Bonilla-Naar. Pp. 245, with several illustrations. Bogota, Columbia, Publications Cientificas.

ANNOUNCEMENT

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The American Urological Association offers an annual award of $1,000.00 (first prize of $500.00, second prize $300.00, and third prize $200.00) for essays on the result of some clinical or laboratory research in Urology. Competition shall be limited to urologists who have been in such specific practice for not more than ten years, and to men in training to become urologists.

The first-prize essay will appear on the program of the forthcoming meeting of the American Urological Association, to be held at the Waldorf-Astoria, New York City, May 31 to June 3, 1954.

For full particulars write the Executive Secretary, William P. Didusch, 1120 North Charles Street, Baltimore, Md. Essays must be in his hands before Feb. 1, 1954.

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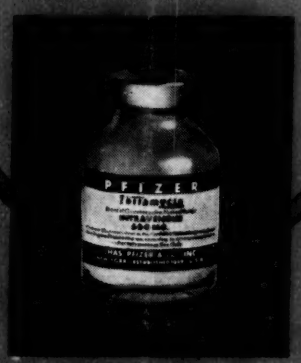
Farley, W. J., Konieczny, L.: J. Pediat. *42*:177 (Feb.) 1953.

Vials of 250 mg. and 500 mg.



as well as adult patients

Intravenous Terramycin, followed by oral therapy after 3-5 days, "is a singly effective, superior antibiotic in the treatment of peritonitis and . . . a good result can frequently be obtained with this drug when [other antibiotics] have failed. It thus has great usefulness both as a primary therapeutic agent and as an alternate antibiotic."

Reiss, E., et al.: A. M. A. Arch. Surg. *64*:5 (Jan.) 1952.

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